TEXT OF PHILIP MORRIS RESPONSE TO OSHA RFI

VOLUME I

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March 18, 1992

Docket Officer
Docket No. H-122
Room N-2625
U.S. Department of Labor
200 Constitution Avenue, N.W.
Washington, DC 20210

Dear Sir or Madam:

Re: Occupational Exposure to Indoor Air Pollutants--
Request for Information

Enclosed herewith are comments submitted on behalf of the Philip Morris family of companies (hereinafter Philip Morris or the Company) regarding the above-referenced matter. We appreciate the opportunity to comment in this proceeding and look forward to participation in subsequent rulemaking activities, in the event the Agency determines that such action is warranted.

The Philip Morris submission consists of three parts. First, because of the length of our overall submission, we have provided an Executive Summary of our comments in order to facilitate Agency review. This Executive Summary is appended as an attachment to this transmittal letter. Second, we have provided a response to the OSHA Request for Information (RFI) background section. This response includes a specific section addressing the 1986 Surgeon General's Report, the NIOSH Current Intelligence Bulletin on ETS, the EPA draft risk assessment, and other risk assessments regarding ETS, as well as a glossary of terms used in our response. Third, we have provided substantive comments in response to OSHA RFI Questions 2a(i), 2a(ii), 2a(iii), 2a(iv), 2d, 3, 5, 6, 7, 8, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 23, 24, 25, 26a, 26b, 29, 33, 34, 35, 36, 37, 38, 39, 40, 41, 43, 45, 46, 47, 48, 49, 50, 51, 54, 55, 56, 61, 62, 63, 64b, 65, 66, 67, 68, 71a, 72, 73, 74, 75a, 75b, 76, 78, 85a, 88, 89, and 92.

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We are committed to working in a constructive and cooperative manner with OSHA in this proceeding. We believe that if OSHA is presented with relevant data, if it views the data completely and fairly, and if it takes the opportunity to observe the various working environments to which its regulatory decisions will apply, the Agency will be in the best possible position to make a decision which protects worker health and safety without placing unwarranted burdens upon American businesses and without unnecessarily intruding on the rights of workers.

Philip Morris Companies Inc. is the largest consumer packaged goods company in the world, with major tobacco, food and beer operations. The Company's operating subsidiaries include Philip Morris Incorporated (U.S.A.), the largest cigarette company in the United States; Philip Morris International, the leading United States exporter of cigarettes; Kraft General Foods, the largest food company in the U.S. and the second largest in the world; and Miller Brewing Company, the second largest brewing company in the world. These companies produce brand name products such as ***Maxwell House, Sanka, Jell-O, Post, Kool-Aid, Marlboro, Entenmann's, Kraft*** cheeses, ***Parkay*** margarine, ***Oscar Mayer, Louis Rich, Breyers, Birds Eye, Cool Whip, Miller High Life*** beer, and ***Lite*** beer. The Company's interests in this matter are (1) as an employer of approximately 166,000 employees of whom approximately 100,000 work in the United States, (2) as the owner and/or manager of over 1,000 buildings, and (3) as the largest manufacturer and exporter of cigarettes in the United States.

We recognize the complexity of the issues relating to OSHA's comprehensive consideration of indoor air quality as reflected in its Request for Information. We also recognize the concerns of some individuals and organizations regarding the issue of environmental tobacco smoke (or, as it is referred to in the Request for Information and will be referenced in the remainder of this submission, passive tobacco smoke [PTS]). We are aware that some people may find smoking objectionable in the work environment. We acknowledge the rights of all employees, and encourage the accommodation of both smokers and non-smokers through tolerance, common sense, and courtesy.

As the Agency undertakes its review of the volumes of data which have already, and will be, submitted in response to its Request for Information, we urge it to do so in a fair and impartial manner, and not to allow issues of personal preference or bias to affect its scientific and technical judgment. We urge the Agency to make decisions that are well-supported by a fair interpretation of the relevant data.

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We again thank you for the opportunity to provide our comments on this issue and offer to assist the Agency further in its deliberations. We look forward to the process.

Sincerely,

CONSTANGY, BROOKS & SMITH

By: _____

Patrick R. Tyson, Esquire
2400 Peachtree Center Building
230 Peachtree Street, N.W.
Atlanta, Georgia 30303
(404) 525-8622

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EXECUTIVE SUMMARY[1]

I. INTRODUCTION

On September 20, 1991, the Occupational Safety and Health Administration (OSHA) published a Request for Information (RFI) concerning "Occupational Exposure to Indoor Air Pollutants" in the Federal Register. 56 Fed. Reg. 47892 et seq. (1991). The stated purpose of this RFI is to gather data so that OSHA could determine "whether regulatory action is appropriate and feasible to control health problems related to poor indoor air quality." 56 Fed. Reg. 47892 (1991). In examining this central issue, OSHA has requested information concerning the health effects of poor indoor air quality, ventilation system performance, and "specific indoor contaminants such as passive tobacco smoke (PTS), radon and bioaerosols" and "their relative contribution to the overall degradation of indoor air quality as well as associated health effects and methods of exposure assessment and mitigation." 56 Fed. Reg. 47892 (1991).

Despite the Agency's stated central objective of examining all aspects of indoor air quality in determining whether

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1. This portion of the Philip Morris submission to Docket No. H-122 is intended only to summarize some of the critical points more fully discussed in its specific responses to the individual Request for Information inquiries. References within this Executive Summary are to the full text of the Company's responses to those individual questions.

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regulatory activity is warranted, we anticipate that a number of individuals and organizations will use the comment mechanism solely as a forum to vent their objections to passive tobacco smoke. This limited focus ignores significant contributors to indoor air quality problems and, in effect, argues that a ban on PTS will "solve the indoor air quality issue." As will be outlined in this summary and addressed fully in the appended substantive responses to the RFI inquiries, the relevant studies that have examined the role played by PTS on indoor air quality in the workplace environment have demonstrated that this role is minimal.

II. THE ROLE OF PASSIVE TOBACCO SMOKE IN INDOOR AIR QUALITY

A. Distinguishing PTS from Other Types of Tobacco Smoke

Before reviewing the scientific literature on "sick building syndrome" and the epidemiologic studies on health effects claimed to be associated with various substances (including PTS) found in many workplace indoor air environments, it is important that a clear understanding exist about the differences among (1) passive tobacco smoke (PTS) (often referred to in the literature as "environmental tobacco smoke" or "ETS"), (2) sidestream smoke (SS), and (3) mainstream smoke (MS). As discussed below, PTS is different in both quality and quantity from MS and SS.

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PTS is an aged and dilute mixture of sidestream smoke (the smoke from the burning end of a cigarette) and exhaled mainstream smoke (the smoke to which the smoker is exposed). PTS, a dynamic, ever-changing mixture which dissipates and undergoes chemical reactions and physical change as it ages, differs both chemically and physically from MS and SS. There is no single definable, reproducibly characterizable entity known as PTS.[2]

Studies indicate that PTS constituents are hundreds to thousands of times more dilute than either SS or MS. As a result, concentrations of PTS constituents often fall below detection limits of current scientific measurement techniques. (See Responses to Questions 2a(iii) and 35.) In addition, as PTS ages, a number of physical and chemical changes take place. As they age, matter evaporates from PTS particles, the particles also coagulate and increase in size, and chemical compounds transfer between the gas and particle phase of the smoke. Decay patterns for constituents of PTS vary over time and are dependent upon physical conditions in the environment.

PTS is not equivalent to either SS or MS. Yet, many studies employ sidestream/mainstream smoke comparisons, ostensibly to demonstrate the kind and quantity of constituents involved in

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2. Baker, R. and Proctor, C., "The Origins and Properties of Environmental Tobacco Smoke," Environ. Intl. (16): 231-245, 1990.

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exposure to PTS. These comparisons are misleading. (See Response to Question 2a(iii).) As was conceded in the 1986 National Academy of Sciences/National Research Council Report on PTS:

> Because the physicochemical nature of ETS, MS, and SS differ, the extrapolation of health effects from studies of MS or of active smokers to nonsmokers exposed to ETS may not be appropriate.[3]

B. PTS and Sick Building Syndrome

"Sick building syndrome" is generally characterized by a number of non-specific complaints which building occupants relate to conditions (usually the air quality) in the building. These complaints include headaches, nausea, coughs, sore eyes and breathing difficulties. Given the visibility of PTS, it is often initially identified as the cause of these complaints and symptoms. Its presence, however, is frequently an indication of poor ventilation, which results in the accumulation of many other indoor air components that may actually be associated with adverse effects. A review of a large number of actual "sick building" investigations reveals that PTS is correlated with complaints in only two to five percent of all sick buildings investigated.

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3. Committee on Passive Smoking, Board of Environmental Studies and Toxicology, National Research Council, National Academy of Sciences, Environmental Tobacco Smoke, Measuring Exposures and Assessing Health Effects, National Academy Press, Washington, D.C.: 7-8, 1986.

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Specifically, analysis of three large databases on sick building syndrome investigations, including databases from Health and Welfare Canada, T.D. Sterling Ltd., and Healthy Buildings International, reveals no significant correlations between IAQ complaints and specific agents. These results are consistent with the sick building investigations conducted by the National Institute of Occupational Safety and Health (NIOSH). In a review of 203 air quality investigations of schools, health care facilities, and government and business offices, NIOSH concluded that tobacco smoke played a contributing role in only 4 (2%) of the building complaints investigated.[4]

In over 50 percent of the sick building cases contained in the above referenced databases, many symptoms and complaints presumably could have been abated by increasing ventilation rates to those comparable to the rates specified in ASHRAE 62-1989. NIOSH officials recently reported on an additional 326 building investigations conducted by the Agency through 1988. Again, consistent with the other public and private databases, NIOSH reported that over 50 percent of its investigations revealed inadequate ventilation as the source of complaints. (See Response to Question 3a.)

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4. Melius, J., et al., "Indoor Air Quality -- the NIOSH Experience," Ann. Am. Conf. Gov. Ind. Hyg., Vol. 10 : 3-7 (1984).

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C. The Scientific Literature on PTS[5]

In the "Background" section of the RFI, OSHA states that workplace exposure to passive tobacco smoke is a "particular concern in matters dealing with indoor air quality" and asserts that:

> A wide range of health effects caused by passive exposure to tobacco smoke has been reported by the Surgeon General, the National Research Council, the Environmental Protection Agency (EPA), and private researchers, as well as by persons reporting health effects due to exposure to passive smoke while at work. These effects range from acute annoyance and eye and respiratory tract irritation to the development of chronic pulmonary disease, cardiovascular disease, and lung cancer.
>
> 56 Fed. Reg. 47892 (1991).

Contrary to the above assertions about the purported health effects of exposure to PTS in the workplace, the available data from published epidemiologic studies are not sufficient to

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5. In an attached document, Philip Morris has responded specifically to the 1986 Surgeon General's report on The Health Consequences of Involuntary Smoking, the Environmental Protection Agency's Draft Risk Assessment, Health Effects of Passive Smoking : Assessment of Lung Cancer in Adults and Respiratory Disorders in Children, the National Institute for Occupational Safety and Health's Current Intelligence Bulletin, Environmental Tobacco Smoke in the Workplace: Lung Cancer and Other Health Effects and several published risk assessments on PTS.

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support the claim that PTS exposure in the workplace is associated with chronic disease in nonsmokers. A primary deficiency in these studies is the lack of reliable exposure data. Published epidemiologic studies which report an association between spousal or parental smoking and chronic disease (e.g., lung cancer, heart disease, etc.) in nonsmokers are not based on actual exposure assessments for PTS. Instead, these studies rely on subjective responses to questionnaires to assess "exposure" rather than on any quantifiable measurement. For example, questionnaire inquiries regarding "spousal smoking," "parental smoking," or "living with a smoker" are used as surrogate determinants for PTS exposure in these studies. Numerous recent studies indicate, however, that such subjective assessments are an extremely unreliable and inaccurate measure of exposure. Furthermore, these questionnaire responses about exposure often vary widely when compared with actual measurements of PTS constituents in the ambient air. (See Response to Question 2a(iii).)

Actual data on nonsmoker exposure to PTS are available in other published literature. These studies, which measure PTS constituent levels, indicate that nonsmoker exposure to PTS under realistic conditions in public places and workplaces is minimal. For example, researchers report little difference in the ambient levels of carbon monoxide or volatile organic compounds in smoking and nonsmoking areas of workplaces and public places, or in homes

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with and without smokers.[6] In other studies, typical measurements of nicotine range from an exposure equivalent of 1/100 to less than 1/1,000 of one filter cigarette per hour.[7] (See Response to

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6. Kirk, P., et al., "Environmental Tobacco Smoke in Indoor Air." In: Indoor and Ambient Air Quality. R. Perry and P. Kirk (eds.). London, Selper Ltd., 99-112, 1988.

   Duncan, D. and Greavey, P., "Passive Smoking and Uptake of Carbon Monoxide in Flight Attendants," JAMA 251(20): 120-21, 1984.

   Cox, B. and Whichelow, M., "Carbon Monoxide Levels in the Breath of Smokers and Nonsmokers: Effect of Domestic Heating Systems," J Epidemiol Community Health 39: 75-78, 1985.

   Girman, J. and Traynor, G., "Indoor Concentrations," JAPCA 33(2): 89, 1983.

   Yocom, J., "Indoor Concentrations," JAPCA 33(2): 89, 1983.

   Nitta, H., et al., "Measurements of Indoor Carbon Monoxide Levels Using Passive Samplers in Korea." In: Indoor Air '90. The Fifth International Conference on Indoor Air Quality and Climate, Toronto, Canada, July 29-August 3, 77-82, 1990.

   Bayer, C. and Black, M., "Thermal Desorption/Gas Chromatographic/Mass Spectrometric Analysis of Volatile Organic Compounds in the Offices of Smokers and Nonsmokers," Biomed and Envir Mass Spect 14(8): 363-367, 1987.

   Proctor, C., et al., "Measurements of Environmental Tobacco Smoke in an Air-Conditioned Office Building," Environ Technol Letters (10): 1003-1018, 1989.

   Godish, T., "Formaldehyde Exposures from Tobacco Smoke: A Review," AJPH 79(8): 1044-1045, 1989.

   Godish, T., "Residential Formaldehyde: Increased Exposure Levels Aggravate Adverse Health Effects," Journal of Environmental Health 53(3): 34-35, 1990.

7. Hinds, W. and First, M., "Concentrations of Nicotine and Tobacco Smoke in Public Places," New England Journal of Medicine 292(16): 844-845, 1975.

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Questions 2a(iii), 24 and 35.) This means that a nonsmoker would have to spend from 100 to 1,000 hours or more in a workplace where smoking was permitted in order to be exposed to the nicotine equivalent of smoking a single cigarette.

D. Health Effects Purportedly Associated with PTS

It is asserted in the Request for Information that the health effects purportedly associated with PTS range from "acute

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7.(...continued)

Badre, R., et al., "Pollution Atmospherique par la Fumee de Tabac (Atmospheric Pollution by Smoking)," Ann Pharm Fr 36(9-10): 443-452, 1978. Translation.

Jenkins, R., et al., "Development and Application of a Thermal Desorption-Based Method for the Determination of Nicotine in Indoor Environments." In: Indoor and Ambient Air Quality. R. Perry and P. Kirk (eds.). London, Selper Ltd., 557-566, 1988.

Muramatsu, M., et al., "Estimation of Personal Exposure to Tobacco Smoke with a Newly Developed Nicotine Personal Monitor," Environ Res 35: 218-227, 1984.

Muramatsu, M., et al., "Estimation of Personal Exposure to Ambient Nicotine in Daily Environment," Arch Occup Environ Health 59: 545-550, 1987.

Thompson, C., et al., "A Thermal Desorption Method for the Determination of Nicotine in Indoor Environments," Envir Sci Tech 23: 429-435, 1989.

Foliart, D., et al., "Passive Absorption of Nicotine in Airline Flight Attendants," New England Journal of Medicine 308(18): 1105, 1983.

Oldaker, G. and Conrad, F., "Estimation of the Effect of Environmental Tobacco Smoke on Air Quality Within Passenger Cabins of Commercial Aircraft," Envir Sci Tech 21: 994-999, 1987.

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annoyance and eye irritation to the development of chronic pulmonary disease, cardiovascular disease and lung disease." We contend that the published research does not support this assertion.

1. Lung Cancer

The argument that PTS exposure increases the risk of lung cancer in nonsmokers is based on data from epidemiologic studies of nonsmoking women married to smokers (spousal smoking). Of the 30 published epidemiologic studies on the issue of spousal smoking and lung cancer, none actually measured exposure to PTS. Twenty-four of the 30 studies report results which are not statistically significant -- that is, their conclusions were consistent with the null hypothesis of no association between reported exposure to PTS and lung cancer in nonsmokers.[8] Only 12 of the published

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8. Despite the inconclusive nature of the epidemiologic data on spousal smoking, several risk assessments estimating excess lung cancer mortality purportedly due to PTS have appeared recently in the published literature. Two approaches have been used. The first attempts to extrapolate risks for the general nonsmoking population based upon the risk rates reported in epidemiologic studies on spousal smoking. One such risk assessment has estimated that as many as 5,000 deaths per year can be attributed to PTS exposure among nonsmokers in the U.S. The second approach estimates a risk for nonsmokers which is based upon the reported dose of tobacco smoke for active smokers.

   Risk assessment models which are based upon dose-extrapolation from the active smoker disregard the physico-chemical differences between mainstream smoke and PTS. This approach also assumes the applicability of linear extrapolation from active smoking to very low estimates of PTS exposure and dose

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spousal studies have assessed reported workplace exposures to PTS at all, but again no actual measurements were conducted. Ten of the 12 workplace studies report associations between PTS and nonsmoker lung cancer which do not achieve statistical significance. Only two studies report marginally statistically significant increased risks for persons who reported exposure to PTS in the workplace. (See Response to Question 2a(iii).)

2. Heart Disease

There are no studies in the published literature which have examined actual PTS exposures in the workplace and heart disease in nonsmokers. Only twelve epidemiologic studies on spousal smoking in the home and heart disease in nonsmokers are available. These studies, based on marriage to a smoker, are not relevant to

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8.(...continued)
for nonsmokers. Dose-extrapolation models which employ unrealistically high estimates of PTS exposure for nonsmokers nevertheless generate mortality projections which are at least an order of magnitude lower than estimates from the epidemiologic-based models. Dose-extrapolation models which are based upon realistic exposure levels of PTS for nonsmokers from actual constituent monitoring studies in homes, public places and the workplace have failed to predict any significant increased risk for nonsmokers.

Both approaches have been criticized extensively in the published literature. In particular, both assessments assume a causal connection between PTS exposure and lung cancer in nonsmokers. Moreover, the risk assessment models which are based upon epidemiologic studies accept uncritically the relative risks reported in studies on spousal smoking. The approach also assumes, without foundation, that these reported risks are attributable solely to PTS.

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the workplace issue. In addition, the spousal smoking studies on heart disease contain no data on actual exposures to PTS. Instead, exposure estimates are derived from questionnaire responses.

Nonetheless, five of the 12 published epidemiologic studies on spousal smoking and heart disease did attempt to address workplace exposures to PTS. However, none of the five studies reported a statistically significant increased risk of heart disease among nonsmokers claiming exposure to PTS in the workplace. Thus, the existing literature does not provide support for the claim that PTS exposure in the workplace is related to an increase in risk of heart disease among nonsmokers.

3. Respiratory Disease Other than Cancer/Asthma

Relatively few studies have examined the possible relationship between reported exposure to PTS in the workplace and the respiratory health of nonsmoking adults. The studies that have been conducted on this issue reported contradictory results. Researchers who have reviewed these studies cited problems with the methodology utilized and pointed out that confounding factors are not adequately controlled for in the studies. (See Response to Question 2a(iii).)

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Data on the possible association between exposure and increased risk of an asthmatic reaction are similarly contradictory. There are nine major studies on the possible association between exposure to PTS and acute respiratory symptoms in adult asthmatics. The studies are inconsistent in their reported results which range from reported decreases in pulmonary function of several asthmatics exposed to PTS to conclusions that PTS exposures present no acute respiratory risks to asthmatics. The studies that do report an association between adult asthma and exposure to PTS suffer from several methodological flaws that include: (1) confounding factors that are not adequately controlled for in many studies; (2) inadequate sample sizes; (3) psychological factors that have not been ruled out; and, (4) reliance on unrealistic exposure conditions in enclosed smog chambers. (See Response to Question 2a(iii).)

III. SOURCES OF INDOOR AIR POLLUTION

PTS receives significant public attention because of its visibility in the indoor environment. However, as discussed above, the role of PTS in the make-up of the overall indoor air quality environment is minimal. In fact, in the RFI itself, OSHA has recognized that a myriad of specific airborne substances in indoor workplaces, often interacting with one another, result in health complaints related to indoor air quality. In many cases, investigations of these complaints have revealed exposure levels

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of the various constituents in indoor air well below established OSHA permissible exposure limits. Perhaps most notably, statistics cited in the RFI from approximately 500 NIOSH Health Hazard Evaluations reveal that while indoor air quality complaints result from numerous airborne substances, the source of most complaints is "inadequate ventilation." The primary types of indoor air quality problems encountered in these investigations were categorized as:

> inadequate ventilation (52%); contamination from inside the building (17%); contamination from outside the building (11%); microbiological contamination (5%); contamination from building materials and furnishings (3%) and unknown sources (12%).
>
> 56 Fed. Reg. 47892 (1991).

In its more detailed study of 203 of these investigations (1984), NIOSH reported that tobacco smoke was a contributing factor in only four (2%) of the buildings investigated. In a 1989 follow-up report of over 500 building investigations, NIOSH did not elect to even designate PTS as a separate category of contributing factors.[9]

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9. U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health, Division of Standards Development and Technology Transfer, "The NIOSH Approach to Conducting Indoor Air Quality Investigations in Office Buildings," Indoor Air Quality Selected References, September, 1989.

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A. Chemical Agents

There is a large body of scientific literature which suggests that exposure to significant levels of chemical agents in the indoor air environment, such as formaldehyde, carbon monoxide, nitrogen dioxide and carbon dioxide, is associated with complaints about adverse health effects. Organic chemical agents, including volatile organic compounds (VOCs), have specifically been implicated as contributors to indoor air complaints. For example, exposure to formaldehyde, which offgasses from some building products, has been associated with irritation of the eyes, skin, and the respiratory tract and has been designated a potential carcinogen in humans. The literature further suggests that exposure to other VOCs has similarly been associated with symptoms of sick building syndrome, such as headaches, dizziness, fatigue, eye, nose and throat irritation, and possibly decreased immunity. Scientists have also reported that there are synergistic reactions that possibly occur between significant levels of different chemical agents in the indoor environment, and that attempts to control individual sources of chemical agents may not be sufficient to prevent this potential combined effect. Moreover, specific VOC levels have been associated with specific health complaints from occupants of buildings with inadequate ventilation. (See Response to Questions 2a(i) and 26a.)

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B. Bioaerosols

In 1984, the New York Academy of Medicine drafted a resolution on indoor air pollution in which they stated:

> By far the most important substances in indoor air that affect human health are infectious agents, primarily viruses and bacteria, in the form of aerosols or as a part of droplets or particles. These cause more than 60,000 deaths and 250 million disabling illnesses in the United States each year. Their effects upon health are many times greater than that of all other indoor air pollutants.[10]

Bioaerosols are biological agents such as viruses, bacteria, mold spores, and fungi. In the indoor environment, the typical health effects associated with bioaerosols are infectious respiratory diseases such as Legionnaires' disease, Pontiac Fever, colds and influenza, and other conditions including hypersensitivity pneumonitis, humidifier fever, asthma, and sick building syndrome. The incidence of many of these illnesses has been linked to improper maintenance of ventilation systems or to inadequate levels of air exchange. For instance, Legionella pneumophila, the organism responsible for Legionnaires' disease, a form of severe, sometimes

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10. Committee on Public Health, New York Academy of Medicine, "Resolution Concerning Federal Legislation and Research on Indoor Air Pollution," Bulletin of the New York Academy of Medicine, 60 : 106-109, 1984.

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fatal pneumonia, has been isolated in water from ventilation systems. Publicly available statistics indicate that a substantial portion (as much as 40%) of buildings may have biological contamination. (See Response to Questions 2a(ii), 5b and 33a.)

C. Radon

Radon is a naturally occurring radioactive gas that is present in both outdoor and indoor environments. Radon is produced by the radioactive decay (breakdown) of uranium. Radon itself decays and produces "progeny" or "daughters," which along with the actual radon, can be inhaled. Epidemiologic studies report an increased risk of lung cancer associated with the inhalation of radon and radon progeny in underground miners. Based on extrapolation from the miner studies, it has been suggested that radon exposure may be responsible for 10-20% of the attributable lifetime lung cancer risk in the general population. Therefore, radon is a major mitigation concern for building owners. (See Response to Question 2a(iv).)

IV. EFFECTIVE VENTILATION AND INDOOR AIR QUALITY

One of the responses to the energy crisis of the 1970s was to reduce the volume of outside air introduced into buildings through their ventilation systems. Although this measure served a

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useful energy conservation purpose, it had the unintended consequence of increasing the incidence of health-related complaints associated with indoor air quality. As specifically noted in the "Background" section of the RFI, OSHA itself has recognized that "[h]ealth complaints related to indoor air quality . . . increased significantly following energy conservation measures instituted in the early seventies. Such measures have generally reduced the infiltration of outside air, allowing the build-up of indoor air contaminants." As discussed above, OSHA has further recognized that of the approximately 500 Health Hazard Evaluations for indoor air quality conducted by NIOSH over the past decade, 52% of the problems encountered were categorized as being due to inadequate ventilation. 56 Fed. Reg. 47892 (1991).

If OSHA determines that regulation of indoor air quality is warranted, the health complaints related to poor indoor air quality may be significantly reduced in a cost effective manner by adopting ventilation rates such as those specified in the American Society of Heating, Refrigerating and Air Conditioning Engineers[11] (ASHRAE) Standard 62-1989, "Ventilation for Acceptable Indoor Air Quality." ASHRAE Standard 62-1989 establishes minimum ventilation rates for various indoor settings in order to "control carbon dioxide and other contaminants with an adequate margin of safety,

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11. ASHRAE is a standard setting group that develops voluntary consensus guidelines for building designers and contractors.

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and to account for variations among people, varied activity levels, and a moderate amount of smoking." This Standard was approved in 1990 by the American National Standards Institute (ANSI). ASHRAE 62-1989 has been adopted by 12 states and by two major building code organizations in the United States, and is currently under consideration for adoption by the remaining national building code organizations. The Standard establishes a ventilation rate of 20 cubic feet of outside air per minute (cfm) per person for most commercial or office facilities, with 15 cfm as the minimum. The drafters of the Standard concluded that a minimum ventilation rate of 15 cfm/occupant will produce air quality that is acceptable to 70% of visitors and to 90% of occupants, assuming a moderate amount of smoking (30% smoking, 1.7 cigarettes/hour/smoker). See ASHRAE Standard 62-1989, "Ventilation for Acceptable Indoor Air Quality," Atlanta, ASHRAE Publications, 1989. Moreover, adoption of the ventilation rates in the current ASHRAE Standard would be consistent with OMB Policy Directive A-119 which instructs government agencies to look to consensus standards when establishing regulations.

The importance of adequate ventilation for achieving and maintaining acceptable indoor air quality should not be underestimated. Ventilation provides a comprehensive solution to

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problems with indoor air quality. As building investigators from Healthy Buildings International have noted:[12]

> Smoke accumulation within offices may be only the tip of the iceberg. If smoke is trapped by bad ventilation so are all other indoor pollutants. Many of these invisible chemicals, dusts, fibers, bacteria and fungi can have acute or long term health effects on the building occupants . . . [R]eacting solely to the visible evidence of poor ventilation omits invisible pollutants and certainly does not address the fundamental problem of inadequate ventilation.

Scientific and technical literature suggests that compliance with ventilation rates specified in ASHRAE Standard 62-1989 will effectively minimize complaints about PTS and other substances in indoor air. For example, in 1990, researchers presented results of their work comparing the effects of increased ventilation recommended by ASHRAE 62-1989 in areas where smoking is permitted and in areas where it is prohibited. Through the aid of computer models, the researchers demonstrated that the quality of air in areas where smoking is permitted does not differ significantly from the quality of air in non-smoking areas, where

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12. "Factors Affecting Employee Health & Comfort: Tobacco Smoke Signals New Challenges for Managers," Healthy Buildings International, September/October, 1991: 2-5.

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both areas are supplied with outside air at the level recommended by ASHRAE 62-1989.[13]

Scientific literature also reveals that increasing the rate of ventilation reduces levels of radon in indoor air. In their study of the reduction of indoor air concentrations of radon, Jonassen and McLaughlin wrote that:

> [T]he most effective way of reducing the activity concentrations of radon and its progeny in the room air is ventilation. Ventilation with radon free (or radon poor) air will, of course, reduce the concentrations of the daughter products directly by dilution.[14]

Not only will compliance with ventilation rates such as those in ASHRAE Standard 62-1989 help to achieve and maintain acceptable air quality in the workplace, but this goal can be accomplished cost effectively. Indeed, if state-of-the-art technology is employed in the design and operation of HVAC systems, ventilation rates at or above those specified by ASHRAE 62-1989 may be provided at reduced operating and energy costs, compared to

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13. Pedelty, J. and Holcomb, L., "A Computer Simulation of Indoor Air Quality Which Models Changes in Point Sources and Ventilation," Environ Technol Letters 11: 1053-1062, 1990.

14. Jonassen, N. and McLaughlin, J.P., "The Reduction of Indoor Air Concentrations of Radon Daughters Without the Use of Ventilation," The Science of the Total Environment 45: 485-492, 1985.

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the operation of traditional systems.[15] However, even in those instances where existing HVAC equipment is operated to deliver ventilation rates in accordance with all specifications in ASHRAE 62-1989, estimates of increased operating costs typically range from only 1% to 8%. Research suggests that even these costs would be offset by the benefits of improved productivity and reduced absenteeism that result from adequate ventilation.[16] In fact, some researchers have argued that the cost of absenteeism attributable to poor indoor air quality greatly exceeds any increased energy expenditures related to compliance with ASHRAE Standard 62-1989.[17] (See Responses to Questions 45, 48, 49, 66, 71, 75a and 85a.)[18]

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15. Electric Power Research Institute, Cold Air Distribution Design Guide, EPRI EM-5730 Project 2732-3, Final Report, March 1988.

16. Goodfellow, H. and J. Wyatt, "Critical Review of Ventilation Contaminants in indoor Air," Indoor Air Quality and Ventilation, ed. F. Lunau, London, Selper Ltd.: 95-104, 1990.

17. The Sheet Metal and Air Conditioning Contractor's National Association, Statement on H1066 "The Indoor Air Quality Act of 1991" to The House Science, Space and Technology Committee, Environment Subcommittee, May 9, 1991; Miller, R., Indoor Air Quality, (Norcross, GA., S.E.A.I. Technical Publications, 1991), 145; Binnie, P., "The Role of Ventilation in Controlling the Quality of Indoor Air, Including ETS," Other People's Tobacco Smoke, ed. A. Armitage, (East Yorkshire (U.K.), Galen Press 1991): 159-172.

18. See Philip Morris' response to RFI Question No. 92 which outlines the elements recommended for regulatory action on indoor air quality, should OSHA determine to promulgate an IAQ standard.

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V. CONCLUSION

We believe the scientific data demonstrate that typical exposures to PTS in the workplace are minimal (See Responses to Questions 24, 35-38), that PTS plays a minor role in "sick-building syndrome" (See Response to Question 3) and that ventilation rates such as those prescribed in ASHRAE Standard 62-1989 result in the maintenance of acceptable indoor air quality in general, including the dilution and removal of PTS and other indoor air constituents (See Responses to Questions 49, 62, 66, 71). There is a significant body of scientific literature which suggests that exposure to chemical agents, radon and bioaerosols in the indoor environment is associated with complaints and possible adverse health effects. Taken together, these data suggest that a focus on PTS in an attempt to address poor indoor air quality would be misdirected and inadequate. In fact, prohibition of smoking would not have affected indoor air quality problems in 95-98% of the building investigations reported to date.

The available data from published epidemiologic studies are not sufficient to support the claim that PTS exposure is associated with chronic disease in nonsmokers. Moreover, virtually all of the published epidemiologic studies that have attempted to address workplace exposure to PTS failed to report a significant

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increased risk of chronic disease in nonsmokers associated with PTS exposure in the workplace.

Thus, to the extent that OSHA determines that a need exists for regulatory action, it is recommended that OSHA frame its regulations in terms of an overall performance standard which will address inadequate ventilation, rather than through efforts to control each specific substance that may be found in indoor air. To this end, the ventilation rates set forth in ASHRAE Standard 62-1989 stand as the most commonly recognized ventilation standard designed to address complaints about indoor air quality. Consideration of this Standard by OSHA is consistent with OMB Policy Directive A-119 which instructs federal regulatory agencies to consider existing consensus standards and guidelines in addressing regulatory issues. Thus, if OSHA determines regulatory action is warranted, adoption of ventilation rates at least equivalent to those set forth in a general consensus standard like ASHRAE 62-1989 would constitute a well-reasoned approach that has been scientifically shown to improve indoor air quality and, at the same time, would allow employers flexibility in accommodating the wishes of their diverse workforces.

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PHILIP MORRIS RESPONSE TO OSHA RFI

Background Statement

Summary:

Several claims about PTS (passive tobacco smoke) exposure which appear in the Background Statement of the OSHA RFI are not scientifically accurate and are not supported by actual data. On the contrary, actual data on exposures to PTS constituents under realistic conditions in the workplace indicate minimal exposures for nonsmokers.

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PHILIP MORRIS RESPONSE TO OSHA RFI

Background Statement

Response:

In its overview statement (Supplementary Information: Background), the OSHA RFI states:[a]

> It has been established in many reports that tobacco smoking is one of the major factors causing poor indoor air quality and that nonsmoker exposure to PTS while at work can be significant. It has also been established that of the more than 3,800 compounds in PTS, 60 are known or suspect carcinogens (Repace and Lowrey 1985).

While several published reviews on PTS have claimed that tobacco smoke is a "major factor causing poor indoor air quality," actual measurements of PTS constituents under realistic conditions in homes, public places and the workplace indicate that contributions of PTS to overall indoor air are insignificant. For example, PTS appears to have little influence on overall carbon monoxide levels, and contributes about 20-30% of the particulate burden in indoor air where smoking takes place.[1-22] Moreover, many measurements of PTS constituents are below the limits of detection for highly sensitive monitoring devices.[1,2,9,10]

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It has also been stated, without adequate scientific support, that PTS exposures "at work can be significant." Studies reporting actual data on PTS constituent levels in the workplace suggest minimal overall exposures for nonsmokers.[1,2,8,9,10]

The claim that "3,800 compounds" are identifiable in PTS is erroneous. This figure is derived from data on constituents of mainstream smoke (the smoke to which the smoker is exposed). PTS, on the other hand, is highly diluted and chemically distinct from mainstream smoke. Similarly, the claim that "60 known or suspect carcinogens" exist in PTS has not been substantiated in the scientific literature.

These claims thus are not supported by scientific data in the published literature on PTS.

The RFI further states:[a]

> Tobacco smoke has been classified as a human carcinogen by the International Agency for Research on Cancer (IARC), the Surgeon General, and the EPA.

It is important to note that each of the respective Agency's classifications of tobacco smoke as a "human carcinogen" was based upon the imputed identification and presence of suspected carcinogens in mainstream smoke and/or fresh sidestream smoke (smoke

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from the burning tip of the cigarette). IARC, the Surgeon General and the EPA did not examine PTS per se; they did not review the available published data on either the characterization of, or the exposure to, PTS. PTS is neither chemically nor physically equivalent to either mainstream or sidestream smoke, and it is therefore not scientifically acceptable to treat mainstream smoke, sidestream smoke and PTS as qualitatively and quantitatively similar mixtures.[23-28]

The most recent classification of tobacco smoke as a "human carcinogen" was proffered by the EPA in its 1990 Draft Risk Assessment. The Draft was heavily criticized and challenged by a number of scientists, most notably for its uncritical reliance on epidemiologic studies and for its failure to examine other relevant data on actual PTS exposures and the chemical/physical characterization of PTS.[b] Furst has recently argued that "the decision to classify a chemical as a human carcinogen must depend upon agreed conclusions from epidemiology, bioassays and some short-term tests; information from only one of these disciplines is inadequate."[c]

IARC, in its classification, conceded that PTS is not equivalent to either mainstream or sidestream smoke and that the epidemiologic data on disease rates among nonsmokers living with smokers are inconclusive. The Agency based its classification, in

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large part, not upon PTS per se but upon imputed "knowledge of the nature of mainstream and sidestream smoke."

In similar fashion, the recent NIOSH Current Intelligence Bulletin's classification of PTS as "a potential occupational carcinogen" was not based upon a critical examination of the physico-chemical composition of PTS per se, or upon any data regarding workplace exposures to PTS or associations between reported exposures and claimed health effects among nonsmokers in the workplace.[e] If the actual data on both PTS exposures and health effects in the workplace are examined, one finds that typical workplace exposures to PTS are minimal and often below limits of detection for even the most sensitive tobacco smoke constituent monitors. In addition, few studies (among many) which examine the possible association between reported PTS exposures and chronic disease (e.g., lung cancer, heart disease, etc.) among nonsmoking workers report statistically significant increased risks.

The extent to which OSHA relies uncritically upon such Agency determinations in its evaluation of PTS issues is a serious scientific oversight.

A full discussion of the 1986 Surgeon General's Report, the EPA Draft Risk Assessment and the NIOSH Current Intelligence Bulletin is provided in the document entitled "Philip Morris

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Comments on the 1986 Surgeon General's Report, the EPA Draft Risk Assessment, the NIOSH Current Intelligence Bulletin, and Other Risk Assessments on PTS."

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REFERENCES*

a. Department of Labor Occupational Safety and Health Administration, "Occupational Exposure to Indoor Air Pollutants; Request for Information," Federal Register 56(183): September 20, 1991.

b. U.S. EPA, "A Brief Summary of the Public Comments Submitted to the U.S. EPA in Response to the External Review Draft EPA 600/6-90/006A," Science Advisory Board Meeting, December 4 and 5, 1990.

c. Furst, A., "Pitfalls in Assessing Risks from Carcinogens," Bio and Env Sciences 4: 1991, 242-249.

d. International Agency for Research on Cancer, "IARC Monographs on the Evaluation of the Carcinogenic Risk Chemicals to Humans: Tobacco Smoking," 38 (Lyon, WHO, 1986).

e. See: Borelli, T., "Comments on NIOSH CIB on ETS," September 19, 1991.

*Copies of these references follow this response at Tabs A-E.

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REFERENCES*

1. Kirk, P., et al., "Environmental Tobacco Smoke in Indoor Air." In: Indoor and Ambient Air Quality. R. Perry and P. Kirk (eds.). London, Selper Ltd., 99-112, 1988.

2. Sterling, T. and Mueller, B., "Concentrations of Nicotine, RSP, CO and CO_2 in Nonsmoking Areas of Offices Ventilated by Air Recirculated from Smoking Designated Areas," Am Ind Hyg Assoc J 49(9): 423-426, 1988.

3. Cox, B. and Whichelow, M., "Carbon Monoxide Levels in the Breath of Smokers and Nonsmokers: Effect of Domestic Heating Systems," J Epidemiol Community Health 39: 75-78, 1985.

4. Duncan, D. and Greavey, P., "Passive Smoking and Uptake of Carbon Monoxide in Flight Attendants," JAMA 251(20): 120-121, 1984.

5. Girman, J. and Traynor, G., "Indoor Concentrations," J Air Pollut Control Assoc 33(2): 89, 1983.

6. Yocom, J., "Indoor Concentrations," J Air Pollut Control Assoc 33(2): 89, 1983.

7. Nitta, H., et al., "Measurements of Indoor Carbon Monoxide Levels Using Passive Samplers in Korea." In: Indoor Air '90: Proceedings of the Fifth International Conference on Indoor Air Quality and Climate. Toronto, Canada, Volume 1, 77-82, July 29-August 3, 1990.

8. Sterling, T., et al., "Environmental Tobacco Smoke and Indoor Air Quality in Modern Office Work Environments," Journal of Occupational Medicine 29(1): 57-62, 1987.

9. Carson, J. and Erikson, C., "Results from Survey of Environmental Tobacco Smoke in Offices in Ottawa, Ontario," Environ Technol Letters 9: 501-508, 1988.

10. Oldaker, G., et al., "Results From Surveys of Environmental Tobacco Smoke in Restaurants." In: Indoor Air Quality. H. Kasuga (ed.). Berlin, Heidelberg, Springer-Verlag, 99-104, 1990.

11. Ogden, M. and Maiolo, K., "Collection and Analysis of Solanesol as a Tracer of Environmental Tobacco Smoke (ETS)." In: Indoor

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* Copies of the references listed herein are supplied in the Philip Morris Response to RFI Question 35.

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and Ambient Air Quality. R. Perry and P. Kirk (eds.). London, Selper Ltd., 77-88, 1988.

12. Proctor, C., "The Analysis of the Contribution of ETS to Indoor Air." In: Indoor and Ambient Air Quality. R. Perry and P. Kirk (eds.). London, Selper Ltd., 57-66, 1988.

13. Eatough, D., et al., "Assessing Exposure to Environmental Tobacco Smoke." In: Indoor and Ambient Air Quality. R. Perry and P. Kirk (eds.). London, Selper Ltd., 131-140, 1988.

14. Proctor, C., et al., "Measurements of Environmental Tobacco Smoke in an Air-Conditioned Office Building," Environ Technol Letters (10): 1003-1018, 1989.

15. Proctor, C., "A Multi-Analyte Approach to the Measurement of Environmental Tobacco Smoke." In: Indoor Air Quality and Ventilation. F. Lunau and G. Reynolds (eds.). London, Selper Ltd, 427-436, 1990.

16. Oldaker, G. and Conrad, F., "Estimation of the Effect of Environmental Tobacco Smoke on Air Quality Within Passenger Cabins of Commercial Aircraft," Environ Sci Technol 21: 994-999, 1987.

17. Hinds, W. and First, M., "Concentrations of Nicotine and Tobacco Smoke in Public Places," New England Journal of Medicine 292(16): 844-845, 1975.

18. Badre, R., et al., "Pollution Atmospherique par la Fumee de Tabac (Atmospheric Pollution by Smoking)," Ann Pharm Fr 36(9-10): 443-452, 1978. Translation.

19. Jenkins, R., et al., "Development and Application of a Thermal Desorption-Based Method for the Determination of Nicotine in Indoor Environments." In: Indoor and Ambient Air Quality. R. Perry and P. Kirk (eds.). London, Selper Ltd., 557-566, 1988.

20. Muramatsu, M., et al., "Estimation of Personal Exposure to Tobacco Smoke with a Newly Developed Nicotine Personal monitor," Environ Res 35: 218-227, 1984.

21. Muramatsu, M., et al., "Estimation of Personal Exposure to Ambient Nicotine in Daily Environment," Arch Occup Environ Health 59: 545-550, 1987.

22. Thompson, C., et al., "A Thermal Desorption Method for the Determination of Nicotine in Indoor Environments," Environ Sci Technol 23: 429-435, 1989.

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23. Baker, R. and Proctor, C., "The Origins and Properties of Environmental Tobacco Smoke," Env Int (16): 231-245, 1990.

24. Löfroth, G., et al., "Characterization of Environmental Tobacco Smoke," Env Sci Technol (23): 610-614, 1989.

25. Reasor, M. and Will, J., "Assessing Exposure to Environmental Tobacco Smoke: Is It Valid to Extrapolate from Active Smoke?," Journal of Smoking Related Diseases 2(1); 111-127, 1991.

26. Proctor, C. and Dymond, H., "The Measurement of ETS Through Adsorption/Desorption Procedures." In: Indoor Air Quality. H. Kasuga (ed.). Springer-Verlag, Berlin Heidelberg, 82-89, 1990.

27. Nystrom, C., et al., "Assessing the Impact of Environmental Tobacco Smoke on Indoor Air Quality: Current Status," Proceedings of the ASHRAE Conference, IAQ '86, April 20-23, 1986, Atlanta, Georgia, 213-233, 1986.

28. Scherer, G., et al., "Importance of Exposure to Gaseous and Particulate Phase Components of Tobacco Smoke in Active and Passive Smokers," Occup Env Health (62): 459-466, 1990.

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PHILIP MORRIS COMMENTS ON THE 1986 SURGEON GENERAL'S REPORT, THE EPA DRAFT RISK ASSESSMENT, THE NIOSH CURRENT INTELLIGENCE BULLETIN, AND OTHER RISK ASSESSMENTS ON PTS

The conclusions of reports by three governmental agencies have been extensively relied upon by various organizations and individuals in discussions of health effects purportedly associated with environmental or "passive" tobacco smoke (PTS) exposure in the workplace. These reports are:

[1] The Health Consequences of Involuntary Smoking,[1] a 1986 report of the Surgeon General (hereinafter 1986 Surgeon General's Report);

[2] Health Effects of Passive Smoking: Assessment of Lung Cancer in Adults and Respiratory Disorders in Children (EPA/600/6-90/006A),[2] a review draft released by the Environmental Protection Agency (EPA) in 1990 (Draft Risk Assessment); and

[3] Environmental Tobacco Smoke in the Workplace: Lung Cancer and Other Health Effects,[3] a Current Intelligence Bulletin issued by the National Institute for Occupational Safety and Health in 1991 (NIOSH CIB).

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These reports have taken on importance in the context of this RFI to the extent that OSHA RFI commenters may try to rely upon these documents (and other published risk assessments, also discussed herein) in urging OSHA to regulate smoking in the workplace. As underscored in the following comments, these review papers do not provide a basis for regulation of smoking in the workplace by OSHA.

1986 Surgeon General's Report

The EPA draft risk assessment and the NIOSH CIB rely extensively on the conclusions of the 1986 Surgeon General's Report on "Involuntary Smoking," the U.S. Public Health Service's eighteenth report, and the fifth report issued during the tenure of C. Everett Koop. The 1986 Surgeon General's Report reached two major conclusions which some may urge are relevant to the workplace smoking issue:

> Involuntary smoking is a cause of disease, including lung cancer, in healthy nonsmokers. (p. vii)
>
> The simple separation of smokers and nonsmokers within the same air space may reduce, but does not eliminate, the exposure of nonsmokers to environmental tobacco smoke. (p. vii)

The Surgeon General's review has been challenged by a number of critics. One reviewer, Ann Fettner, suggested that the

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Surgeon General's conclusions were based on "flimsy" evidence presented in an effort to "divert our attention" from important health concerns such as the "poisoning of the environment."[4] A U.S. Congressman, Walter B. Jones, in a letter published in the Congressional Record, wrote that "the conclusions in the Surgeon General's Report are not supported by the research in his own report."[5] The Surgeon General's conclusions regarding lung cancer, cardiovascular disease, adult respiratory disease, and separation of smokers and nonsmokers are relevant to OSHA's current considerations of the workplace environment and will be discussed below in some detail.

Lung Cancer

The Surgeon General's conclusion that a causal relationship exists between PTS exposure and lung cancer in nonsmokers was based on 13 epidemiologic studies of women whose husbands smoked. Of those studies, eleven reported risk estimates that were not statistically significant.[6] Moreover, scientific deficiencies in the epidemiologic studies on PTS and nonsmoker lung cancer have been identified by numerous individuals. A German specialist in biometrics and epidemiology, Karl Uberla, in his assessment of these studies, suggested that the data fail to meet the criteria which some regard as necessary to establish a causal relationship:[7]

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> The majority of criteria for a causal connection are not fulfilled. There is no consistency, there is a weak association, there is no specificity, the dose-effect relation can be viewed controversially, bias and confounding are not adequately excluded, there is no intervention study, significance is only present under special conditions and the biologic plausibility can be judged controversially.

An eminent American statistician, Nathan Mantel, has also observed:[8]

> [I]t is unlikely that any epidemiological study has been, or can be, conducted which could permit establishing that the risk of lung cancer has been raised by passive smoking. Whether or not the risk is raised remains to be taken as a matter of faith according to one's choice.

There are currently 30 spousal smoking studies, 24 of which report risk estimates that are not statistically significant.[9-38] Only six studies report statistically significant increased lung cancer risks for women whose husbands smoke. Thus, these studies taken as a group, or considered individually, do not convincingly support rejection of the null hypothesis of no association between PTS exposure and lung cancer in nonsmokers, and therefore are inadequate as a basis for regulatory action.

Moreover, the vast majority of the spousal smoking studies report risk estimates that are less than 2.0. These values are at the limit of detection for epidemiology. Risk estimates below 2.0

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or 3.0 have been described as "weak," and thus, any conclusions drawn from such studies are unreliable.[39] This is particularly true when the studies themselves fail to account for numerous sources of bias and confounding factors. The confounding factors are variables associated with both the classification of "marriage to a smoker" and with risk factors associated with lung cancer, the existence of which can give rise to a spurious PTS-lung cancer association. Examples of confounding factors that are not controlled for in the studies include diet, alcohol consumption, cooking and heating methods, occupation, physical activity, urbanization and socioeconomic class.[40]

In addition, application of spousal smoking studies to the workplace presents significant questions. Even the Surgeon General conceded that "[m]ore accurate estimates for the assessment of exposure in the home, workplace, and other environments are needed" (p. 101).

In fact, the epidemiologic studies on lung cancer and respiratory disease cited in the Surgeon General's Report did not include any actual measurements of study subjects' exposure to PTS in either the home or the workplace. Instead, the studies relied on questionnaire information to estimate exposure to PTS. The Surgeon General's Report itself acknowledges that the "possibility of reporting bias must be considered for the studies

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that have used questionnaires to measure illness experience" (p. 38). A number of researchers have reported that exposure misclassification can lead to improper indices of exposure and incorrect estimations of risk.[10,41-46] The Surgeon General's Report also concedes that "validated questionnaires are needed for the assessment of recent and remote exposure to environmental tobacco smoke in the home, workplace, and other environments" (p. 107). The National Research Council and other authors have recently criticized questionnaires used in PTS studies for not being standardized or validated, pointing out that misclassification of exposure may occur if the questionnaire is not appropriately designed.[47-49]

Separation of Smokers and Nonsmokers

The Surgeon General's Report also concluded that "simple separation of smokers and nonsmokers within the same air space may reduce, but does not eliminate, exposure of nonsmokers to environmental tobacco smoke" (p. vii). The Report concludes that smoking bans will not only reduce PTS exposures, but will also "alter smoking behavior and public attitudes about tobacco use" (p. 322). The Report further suggests that "over time, this may contribute to a reduction of smoking in the United States" (p. 322). Thus, the underlying motivation for the use of the PTS/health argument is to attain a "smoke-free society by the year 2000."

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The Surgeon General's claim that separation of smokers and nonsmokers does not minimize nonsmoker exposure to PTS is without scientific support. Studies aboard commercial aircraft and in offices indicate, contrary to the Surgeon General's Report, that the simple separation of smokers and nonsmokers effectively minimizes nonsmoker exposure to PTS.[50-57] One recent study, for example, reported that the use of designated smoking areas reduced exposure to PTS by 95 percent.[50] Another study of a smoking-restricted office building reported that ambient nicotine in nonsmoking areas was virtually undetectable, suggesting that PTS had a negligible impact on the nonsmoking areas in the building.[51] In addition, Canadian researchers Sterling, et al., in a series of studies, collected data on levels of PTS constituents in offices with different smoking policies. They reported no significant differences in average PTS constituent levels between nonsmoking offices that received recirculated air from designated smoking areas and nonsmoking offices that did not receive recirculated air.[52-53,57] They concluded:

> The results indicate that the provision of a designated, but not separately ventilated smoking area can effectively eliminate or drastically reduce most components of environmental tobacco smoke from nonsmoking offices.

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Adult Respiratory Disease

The Surgeon General's Report also addressed purported changes in pulmonary function in adults reportedly exposed to PTS. The Surgeon General concluded that

> healthy adults exposed to environmental tobacco smoke may have small changes on pulmonary function testing, but are unlikely to experience clinically significant deficits in pulmonary function as a result of exposure to environmental tobacco smoke alone. (p. 13)

Two major research groups have examined the possible association between exposure to PTS in the workplace and pulmonary function in adult nonsmokers. White and Froeb reported, based on their measurements of the small airways function of smokers and nonsmokers in the workplace, that nonsmokers exposed to tobacco smoke at work for 20 or more years had reduced function of the small airways compared to nonsmokers who did not have such exposures.[58]

The White and Froeb study has been criticized for numerous reasons, including its assessment of PTS exposure and its method of subject selection.[59-62] Furthermore, White and Froeb themselves noted that the average values of the pulmonary tests of nonsmokers exposed to tobacco smoke "were not notably different" from the values suggested as normal by a specialist in this area.[63] Dr.

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Michael Lebowitz of the University of Arizona wrote the following regarding the White and Froeb study:[64]

> Even with a biased population, poor study design, and incorrect statistical evaluation, there were no clear-cut, consistent, medically meaningful differences between passive smokers and groups of nonsmokers; a corrected statistical analysis strengthened this conclusion.

Moreover, the Surgeon General wrote:

> The [White and Froeb] study population was self-selected, and the exposure classification was crude and did not account for people who changed jobs. (p. 60)

In addition to these concerns, the results of White/Froeb appear to be inconsistent with those of a second research group, Kentner, et al., who reported no effect of PTS on pulmonary function measurements among 1,351 German office workers.[65] In a 1988 update of the study, Kentner and colleagues noted that[66]

> there is no evidence that average everyday passive smoke exposure in the office or at home leads to an essential reduction of lung function in healthy adults.

The key investigator for the study reported these same findings in 1989 and 1990 publications.[67,68]

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The Surgeon General's Report also addressed the issue of acute effects on the pulmonary function of adult nonsmokers exposed to PTS, the Surgeon General concluded that "the magnitude of these changes is quite small, even at moderate to high exposure levels, and it is unlikely that this change in airflow, per se, results in symptoms" (p. 63). The studies available on asthmatic adults are clinical studies that have potential applicability to the home and the workplace setting. However, the studies that have reported an association between exposure to PTS and reactions in asthmatics have several problems. Regarding the studies on asthma in adults, the Surgeon General wrote:

> Acute exposure in a chamber may not adequately represent exposure in the general environment. Biases in observation and the [sic] in selection of subjects and the subjects' own expectations may account for the widely divergent results. Studies of large numbers of individuals with measurement of the relevant physiologic and exposure parameters will be necessary to adequately address the effects of environmental tobacco smoke exposure on asthmatics. (p. 65)

Cardiovascular Disease

The Surgeon General's 1986 conclusion on cardiovascular disease and PTS was that further studies "are needed in order to determine whether involuntary smoking increases the risk of cardiovascular disease" (p. 14). In 1988, Fielding, et al., reviewers from the University of California-Los Angeles, who are

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critical of smoking, conceded that "no firm conclusion that a causal relation exists is yet warranted" for reported PTS exposures and cardiovascular disease.[69] A similar view was expressed in a 1988 review from a Harvard physician, who said that there were "no clear data" that PTS increases heart disease risk.[70]

Several additional evaluations of the literature on PTS and heart disease appeared in 1990. Two of these were reported at international conferences in Lisbon, Portugal[71] and in Budapest, Hungary.[72] Both argued strongly that the data on PTS and heart disease were methodologically weak and insufficient to draw conclusions. In another major review, this one from the United States, two physicians, Drs. Mahajan and Huber, concluded that "the data that are available are so sparse that any attempt to reach a definitive assessment would be fraught with uncertainty."[73] Perhaps the most recent review of the literature on PTS and heart disease was published in 1991 by A.K. Armitage, the former director of toxicology of a major European research laboratory.[74] He described the scientific data relating to a possible heart disease risk in nonsmokers exposed to PTS as "not very convincing."

In summary, the Surgeon General's claims that exposure to PTS increases the risk of lung cancer in nonsmokers and that simple separation of smokers and nonsmokers is ineffective in minimizing exposure are not convincingly supported by the scientific

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data and should not be used as a basis for workplace smoking policy decisions.

EPA Draft Risk Assessment

In June, 1990, the United States Environmental Protection Agency (EPA) released for review its Draft Risk Assessment on PTS.[2] The Draft Risk Assessment concluded that exposure to PTS is causally related to lung cancer in adult nonsmokers and is associated with respiratory disease and respiratory symptoms in children. The Draft Risk Assessment also concluded that PTS should be classified as a Group A ("known human") carcinogen. It estimated that PTS exposures are responsible for 3,800 lung cancer deaths per year in the U.S. (the estimate was later revised to 3,700).

The Draft Risk Assessment employed a Population-Attributable Risk model for estimating excess lung cancer mortality among nonsmokers reportedly exposed to PTS.[2] This model is based upon three estimates:

1. a point estimate or relative risk derived from a meta-analysis of epidemiologic studies on spousal smoking;
2. the proportion of nonsmokers reportedly exposed to PTS; and
3. the number of nonsmokers in the general population.

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To calculate the Population-Attributable Risk (PAR), the authors of the Draft Risk Assessment estimated that 60% of nonsmokers are exposed to PTS. A cumulative relative risk of 1.28 was calculated via meta-analysis from epidemiologic studies on spousal smoking as the excess risk due to PTS exposure. The PAR for these two assumptions is 0.27. The total number of deaths for nonsmoking males and females was then estimated, based on the American Cancer Society's projections for 1988 (9,500 total deaths). By multiplying the PAR (0.27) by 9,500, the authors generated an estimate of 2,560 total deaths per year attributable to PTS exposure among neversmokers. A PAR was also computed for male and female former smokers, generating a total estimate of 3,800 excess deaths annually purportedly attributable to PTS exposure among nonsmokers in the U.S.

The PAR method employs estimates of relative risk, population fractions of exposure to PTS and lung cancer death rates for the general nonsmoking population in order to generate an estimate of excess mortality reportedly attributable to PTS exposure. It is important to note at the outset that the PAR model itself does not determine that there is an increased risk of lung cancer among nonsmokers from PTS exposure. Rather, the model assumes a causal relationship between PTS exposure and an increased risk of lung cancer among nonsmokers, based upon increased risks

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reported in epidemiologic studies on spousal smoking. These reported relative risks are, in turn, assumed to represent true relative risks due to PTS exposure.

These critical assumptions have been challenged.[75] To achieve a cumulative excess risk estimate of 1.28 for nonsmokers reportedly exposed to PTS, the authors of the Draft Risk Assessment performed a meta-analysis of 23 epidemiologic studies on spousal smoking. However, eighteen of the studies on spousal smoking included in the EPA's meta-analysis fail to achieve statistical significance and are, therefore, consistent with the null hypothesis of no association between spousal smoking and an increased risk of lung cancer among nonsmokers. Moreover, the epidemiologic studies on spousal smoking contain no actual exposure data on PTS. The EPA Draft instead assumed the validity of questionnaire responses about possible exposure to PTS based upon spousal smoking and then generalized these responses to the general population's exposure to PTS. Finally, the authors of the Draft Risk Assessment failed to consider and adjust for confounding factors, e.g., diet, lifestyle, genetics, etc., in any of the individual studies on spousal smoking. This is a significant oversight, especially when dealing with a "weak" relative risk which approximates 1.3.

The Draft's assumption of causality is based upon tenuous data from epidemiologic studies on spousal smoking. The assumption

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is the critical element to the PAR model and the estimate of 3,800 excess nonsmoker deaths per year reportedly due to PTS exposure. The Draft Risk Assessment fails to argue convincingly for the assumption. Without the causal assumption, the PAR approach is little more than an exercise in mathematical modeling.

Furthermore, the conclusions of the Draft Risk Assessment have been strongly criticized, particularly in many of the more than 100 comments submitted during the public comment period on the draft.[75] Specifically, many of the public comments found EPA's classification of PTS as a Group A carcinogen to be scientifically unwarranted.

EPA's proposed classification of tobacco smoke as a "human carcinogen" was based in part upon the imputed identification and presence of suspected carcinogens in mainstream smoke and/or fresh sidestream smoke. However, the EPA apparently did not review the available published data on either the characterization of, or exposure to, PTS. PTS is neither chemically nor physically equivalent to either mainstream or sidestream smoke, and it is therefore not scientifically acceptable to treat PTS, mainstream smoke and sidestream smoke as qualitatively and quantitatively similar mixtures.[76-81] (See also Responses to Questions 2a(iii) and 35.)

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As discussed above, meta-analysis, a statistical procedure which combines the reported risk estimates from a number of studies to generate an overall estimate of risk, was used in the EPA's Population-Attributable Risk model. The problems and limitations of the use of meta-analysis for epidemiologic studies have been addressed in the scientific literature.[82,83] For instance, meta-analysis does not account for intrinsic bias and confounding in the individual studies. As two German scientists, Heinz Letzel and Karl Uberla, noted: "Combining risk estimates from biased or confounded studies by meta-analysis cannot provide correct answers."[83] The spousal smoking studies were conducted in the United States, Europe and Asia. These populations differ genetically and in lifestyle factors, and the studies themselves differ in design.[82]

Another major criticism of the Draft Risk Assessment was that in addition to its inadequate treatment of the data on the physical and chemical properties of PTS, it also virtually ignored the available exposure data, toxicological data and data from animal studies on PTS. For instance, not one of the spousal smoking studies included actual measurements of PTS exposure; exposure was only estimated by responses to questionnaires. However, a large body of literature exists on actual measurements of PTS in indoor environments, which was not considered in the Draft Risk Assessment.[52,76,84-87] While these data are independent of the epidemiologic

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literature, they suggest that nonsmoker exposure to PTS in typical public places and workplaces is minimal.[52,84-87] (See Response to Question 2a(iii).) For example, some studies report typical measurements of nicotine ranging from an exposure equivalent of 1/100 to less than 1/1,000 of one filter cigarette per hour.[56,88-94]

Thus, the conclusions of the EPA's Draft Risk Assessment are based on an incomplete and selective review of the existing data on PTS. Several of the public comments suggested that this amounted to EPA's apparent failure to follow its own guidelines for carcinogen risk assessment.[75]

NIOSH Current Intelligence Bulletin

In June 1991, NIOSH released Current Intelligence Bulletin 54 on environmental tobacco smoke.[3] The NIOSH CIB stated that:

> NIOSH has determined that the collective weight of evidence (i.e., that from the Surgeon General's reports, the similarities in composition of MS and ETS, and the recent epidemiologic studies) is sufficient to conclude that ETS poses an increased risk of lung cancer and possibly heart disease to occupationally exposed workers. (p. 12)

In the excerpt above, the CIB refers to three areas that contribute to its "collective weight of evidence." The Surgeon

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General's report is the first area; however, the conclusions of the Surgeon General's report have been extensively criticized, as discussed above. As for the second type of "evidence" (the claimed "similarities in composition of MS and ETS"), the treatment of the available data in the NIOSH CIB is neither detailed nor complete.

Although the NIOSH CIB and the EPA Draft Risk Assessment stress the reported association between active smoking and disease in reaching their conclusions about PTS, neither report provides detailed discussions of the chemical and physical natures and differences between PTS and mainstream smoke (MS). PTS is different in both quality and quantity from both mainstream and sidestream smoke. (See Responses to Questions 2a(iii) and 35.)

One major area overlooked by both the NIOSH CIB and the EPA Draft Risk Assessment is those scientific studies that actually measured levels of PTS constituents in indoor air. There is a substantial body of literature in this area which is directly relevant to considerations about non-industrial workplace exposure. If the actual data on PTS exposures in the workplace are examined, one finds that typical workplace exposures to PTS are minimal and often below limits of detection for even the most sensitive tobacco smoke constituent monitors. (See Response to Question 2a(iii).)

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The final aspect of NIOSH's "weight of the evidence" is "recent epidemiologic studies" on PTS and lung cancer. However, its review of the spousal smoking studies is incomplete. The CIB states that eight additional spousal smoking studies have been published since 1986, when, actually, 14 have been published, most of which report associations which do not achieve statistical significance. Furthermore, the CIB acknowledges serious shortcomings in the available epidemiologic studies purporting to relate PTS exposure and lung cancer:

> NIOSH recognizes that these recent epidemiologic studies have several shortcomings: lack of objective measures for characterizing and quantifying exposures, failure to adjust for all confounding variables, potential misclassification of ex-smokers as nonsmokers, unavailability of comparison groups that have not been exposed to ETS, and low statistical power.

Nevertheless, the CIB uses spousal smoking studies to reach its conclusion about occupational exposure to PTS without justifying the relevance of spousal smoking studies to workplace exposure. Of the spousal smoking studies, none actually measured levels of PTS to which the subjects ostensibly were exposed. The NIOSH CIB also fails to address the 12 spousal smoking studies that included specific questions about workplace exposure.[9-20] Of those studies, ten reported no statistically significant increased risk of lung cancer for nonsmokers who reported PTS exposure in

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the workplace. The other two studies presented risk estimates which were of borderline statistical significance. Thus, the epidemiologic data are consistent with the null hypothesis, i.e., that there is no association between workplace PTS exposure and nonsmoker lung cancer.

The CIB also purports to review the studies on PTS and heart disease that have appeared since 1986, at which time the Surgeon General remarked that more studies were needed before a conclusion of an association could be made. While additional studies have been published since 1986, taken as a whole, the studies still do not allow a conclusion to be reached.[95] Moreover, the epidemiologic studies on PTS and heart disease may be criticized for several reasons: they use spousal smoking as a surrogate for PTS exposure, they do not have clinical diagnoses of heart disease (e.g., they rely on death certificate data or self-reported symptoms), and they fail to adequately account for confounding factors. The latter include family history of heart disease, blood pressure, serum lipoprotein levels, body mass index, age, menopausal status, dietary fat, alcohol consumption, diabetes and lifestyle factors (e.g., a sedentary lifestyle).

Thus, the NIOSH CIB, which reaches conclusions about purported risks associated with exposure to PTS in the workplace, is not a comprehensive, critical review of the available data.

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Of even greater significance, it does not address available workplace data on exposures or potential health effects.

Other Risk Assessments on PTS

Two basic methods (modeling procedures) for estimating the population risk for lung cancer among nonsmokers reporting exposure to PTS have appeared in the scientific literature. The first method, adopted by the U.S. EPA in its Draft Risk Assessment (discussed above), is the Population-Attributable Risk (PAR) approach. A PAR model seeks to establish an estimate of excess risk due to PTS exposure and is expressed as a ratio of the risk assessed for PTS to the total lung cancer risk for nonsmokers from all sources. The PAR is calculated by applying a relative risk estimate associated with reported exposure to PTS (derived from risk rates in epidemiologic studies) to the percentage of individuals believed to be exposed to PTS in the general population.

A second approach used in the literature, called the Extrapolation Method (also called the Linear Extrapolation Method or Dose-Response Extrapolation Model), combines reported risks of lung cancer for active smokers, derived from epidemiologic studies on smokers, with estimates of tobacco smoke exposure (dose) for active smokers. The risk and dose estimates for active smokers are then extrapolated downward to apply to nonsmokers. The

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estimated excess risk for nonsmokers exposed to PTS is obtained by dividing the lung cancer risk reported for active smokers by the ratio between the smokers' and nonsmokers' estimated average exposure to tobacco smoke.

This second approach for estimating excess lung cancer deaths among nonsmokers reportedly due to ETS exposure is exemplified by the model developed by Repace and Lowrey (1985).[96] The authors employed a linear downward extrapolation from the lung cancer risk reported for active smokers (and estimates of tobacco smoke exposure for smokers) to an exposure and residual risk estimate for nonsmokers allegedly exposed to PTS. The model estimated lung cancer mortality among nonsmokers by dividing the reported lung cancer risk for active smokers by a ratio of estimated tobacco smoke exposure for smokers and nonsmokers. The linear dose-extrapolation model therefore requires four estimates:

1. the number of nonsmokers supposedly exposed to PTS;
2. the average PTS exposure of nonsmokers;
3. the average tobacco smoke exposure for active smokers; and
4. the lung cancer risks reported for current active smokers.

Specifically, Repace and Lowrey developed a version of a linear dose-response extrapolation model which is based upon a

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weighted average of nonsmoker exposure to particulates. The weighted average estimate was not derived from actual exposure data but from a model which predicts ambient concentrations of particulate matter from the number of cigarettes smoked in a given volume of air space. The authors also calculated a lung cancer risk estimate and an estimate of daily "tar" (particulate) intake for active smokers. Nonsmoker risk of lung cancer was extrapolated from those estimates to yield 555 lung cancer deaths per year attributable to PTS exposure among nonsmokers.

Arundel, et al., (1987) refined the Repace and Lowrey extrapolation model by replacing Repace and Lowrey's estimates of particulate matter exposure for nonsmokers with actual exposure data from monitoring studies.[97] The Arundel, et al., model also rejected Repace and Lowrey's extrapolation from the dose of active smokers to the exposure of nonsmokers, and replaces the latter with an estimated retained dose of particulates for nonsmokers. Using virtually the same assumptions as Repace and Lowrey, the Arundel et al. model estimates 12 lung cancer deaths per year among 40 million male and female neversmokers.

The various assumptions and estimates employed in the Repace and Lowrey linear dose-extrapolation model have been challenged by a number of scientists.[97-101] One scientist noted that the exposure and dose levels Repace and Lowrey used were not

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based on actual measurements, and that actual measurements reported by other researchers ranged from "ten-to-one-hundred-fold less than that in the Repace and Lowrey model."[98]

Still other scientists have questioned the methods of analysis used in their article.[99-101] For example, the Repace and Lowrey extrapolation model assumes that the carcinogenicity of tobacco smoke depends upon some (unknown) element purportedly located in the particulate phase of PTS. The model also assumes that lung cancer per unit of exposure (i.e., per mg of "tar") is the same for mainstream smoke and PTS, an assumption which is not borne out by the scientific data regarding the chemistry of mainstream smoke and PTS. Moreover, the extrapolation model suggests that the relationship between reported risk and level of exposure is linear (i.e., dose-response), and it assumes that there is no exposure level below which lung cancer risk is absent. The dose-extrapolation model also assumes, with its suggestion of a linear dose-response from active smoking to low level exposure to PTS, that the so-called "one-hit" cancer theory, a theory that one molecule of exposure to a suspected carcinogen is sufficient to induce carcinogenesis, is valid. However, the "one-hit" model has what statisticians call a "zero intercept term," which is equivalent to assuming that lung cancer risk among nonsmokers is zero <u>in the absence of ETS</u>.

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Even with its dubious assumptions and estimates, it is noteworthy that the linear dose-extrapolation model produces estimates of excess lung cancer deaths which are roughly an order of magnitude lower than estimates generated by the PAR model which relies on epidemiologic studies. A number of subsequently published extrapolation models, unlike that of Repace and Lowrey, have been based upon actual data and reasonable estimates of exposure.[97,102-104] These models have been unsuccessful in estimating any appreciable increased risk of lung cancer for nonsmokers reporting exposure to PTS. Indeed, extrapolation models based on estimates of retained particulate matter generate estimates of excess risk which are as much as 20 orders of magnitude lower than estimates generated by the PAR method. Such vast ranges underscore the difference between risk estimates based on epidemiology and those based on dosimetry. This difference is so striking that even the authors of the EPA Draft Risk Assessment were unable to generate a "dose-response based on the extrapolation from mainstream to environmental tobacco smoke," and hence, relied solely upon the PAR model to support their contention of an increased risk of lung cancer among nonsmokers reportedly exposed to PTS.[105]

There have been two published risk assessments of environmental tobacco smoke (ETS) exposure and heart disease, the first by A. Judson Wells in 1988,[106] and the second by Kyle Steenland in 1992.[107] However, despite his never having published

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a risk assessment on ETS and heart disease, Stanton Glantz is the individual most often cited for the conclusion that a large number of annual heart disease deaths in the U.S. are attributable to ETS exposure. In a 1991 article with William Parmley,[108] Glantz claimed that the number of annual ETS-related nonsmoker deaths in the U.S. is approximately 53,000, the largest portion of which (37,000) he claimed was from heart disease.

The figure of 53,000 annual U.S. deaths attributed to ETS exposure originated in a publication by A. Judson Wells in 1988,[106] although Wells actually argued for a "best estimate" of ETS related deaths that was somewhat lower, about 46,000, with 32,000 of these due to heart disease. Stanton Glantz and William Parmley repeated the 53,000 figure in their 1991 article in Circulation. However, they did not themselves independently perform a calculation of "excess" deaths, but instead relied on the earlier work by Wells, which is cited by Glantz and Parmley as the basis for their claim.

To calculate excess deaths due to ETS exposure, Wells used meta-analysis to derive ETS-associated relative risks for lung cancer, heart disease and cancers other than the lung. These relative risks, together with an estimate of the fraction of the population exposed to ETS, were entered into an equation that was used to calculate excess death rates for never smokers. To derive a value of actual numbers of deaths related to ETS exposure, these

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excess death rates were multiplied by the number of people in the U.S. estimated to be exposed. Based on such calculations, Wells estimated that ETS exposure produced 39,000 excess deaths per year in the U.S.

Further calculations attempted to take into account misclassification, either of smokers as nonsmokers or of nonexposed nonsmokers as exposed to ETS. Wells calculated that these adjustments for misclassification resulted in a revision upward of the estimate, from 39,000 to 53,000. Wells then stated that a more "conservative" estimate would be 46,000, a value chosen because it is halfway between the unadjusted value of 39,000 and the adjusted value of 53,000.

It is clear that the claim of 53,000 excess deaths associated with ETS exposure is assailable at every level of its derivation. At the most fundamental level, the studies contributing to the meta-analysis are scientifically flawed. The flaws stem from, among other reasons, small sample sizes, inadequate control for potential confounding factors and unreliable estimates of ETS exposure. Such flaws contribute to the invalidity of the subsequent meta-analysis, a technique which is further called into question because it is not designed to bring together such methodologically disparate studies. Furthermore, any overall estimate of the prevalence and levels of ETS exposure within the U.S. is based on

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assumptions, rather than direct measurement. In addition, a variety of other unproven assumptions are made in attempting to adjust the data to take potential misclassification into account. Finally, the seemingly capricious derivation of the annual death rate claim is reflected in Wells' final calculation in which he decided, based on no particular formula, that the value of 46,000 would be a "best estimate," simply because it was halfway between an unadjusted and adjusted estimate. Such loose and unscientific conclusions should not form a basis for regulatory action.

Kyle Steenland, a National Institute for Occupational Safety and Health employee, also performed a risk assessment of ETS and heart disease, published in 1992.[107] He calculated that 35,000-40,000 annual U.S. heart disease deaths are attributable to ETS exposure. He concluded that "heart disease mortality is contributing the bulk of the public health burden imposed by passive smoking."

There are two important differences between Steenland's estimation process and that used by Wells. First, Steenland did not do a meta-analysis to obtain a pooled estimate of relative risk for heart disease mortality associated with ETS exposure. Instead, he simply adopted the relative risk reported in a single study of a Maryland sample[109] and applied that to the entire U.S.

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population. Second, he focused only on heart disease and did not attempt to calculate ETS-related deaths from other diseases.

Other than the above, Steenland's procedure for calculating deaths attributable to ETS exposure was generally similar to that reported by Wells. This estimation process involved: positing an overall increase in relative risk of heart disease associated with ETS exposure; making adjustments for potential misclassification and for background exposure; estimating the extent of exposure to ETS; and estimating the fraction of nonsmoker heart disease deaths attributable to ETS exposure. These estimates were incorporated into a formula using data on U.S. heart disease death rates and population estimates, from which was derived an estimated number of annual heart disease deaths attributed to ETS exposure. According to Steenland's calculations, "the overall estimate of ETS-attributable heart disease deaths for never-smokers and former smokers is 35000 to 40000." He further commented that these increased risks of death "are higher than those accepted in regulating environmental toxins."

Steenland's calculations involved problems similar to those that plagued Wells' attempt to derive a number of deaths associated with ETS exposure. Although Steenland cannot be criticized for performing an invalid meta-analysis (because he did no meta-analysis at all), his procedure can perhaps be criticized

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even more severely because he took a relative risk based on a single study from a single county in a single state and applied it to the United States as a whole. Criticisms relating to unverified assumptions, which were noted in regard to Wells' calculations, also apply to Steenland's procedure.

Summary

The conclusions of these governmental reports and other publications are extensively relied upon by those who claim that there is a possible association between PTS exposure in the workplace and adverse health effects in nonsmokers. However, these reports and assertions have serious deficiencies that make their conclusions difficult to support. When appropriate scientific scrutiny is exercised, these reports and articles do not provide a defensible basis for the regulation of smoking in the workplace by OSHA.

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REFERENCES

1. U.S. Department of Health and Human Services, Public Health Service, Office on Smoking and Health, The Health Consequences of Involuntary Smoking: A Report of the Surgeon General. DHHS Publication No. (CDC) 87-8398, Washington, D.C., U.S. Government Printing Office, 1986.

2. U.S. Environmental Protection Agency, Office of Health and Environmental Assessment, Office of Atmospheric and Indoor Air Programs, Health Effects of Passive Smoking: Assessment of Lung Cancer in Adults and Respiratory Disorders in Children, External Review Draft, EPA/600/6-90/006A, May, 1990.

3. U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health, Current Intelligence Bulletin 54: Environmental Tobacco Smoke in the Workplace: Lung Cancer and Other Health Effects. DHHS (NIOSH) Publication No. 91-108, Cincinnati, Ohio, June, 1991.

4. Fettner, A., "Where There's Smoke There's Fire -- The New 'Passive Smoking' Rules: Sidestepping Issues by Scapegoating Smokers," Voice, 5-7, March 30, 1987.

5. Jones, W., "Inconclusive Evidence on the Harmful Effects of Smoking," U.S. Congressional Record - Extension of Remarks, E489-E490, February 18, 1987.

6. Schwartz, S.L. and Balter, N.J., "ETS-Lung Cancer Epidemiology: Supportability of Misclassification and Risk Assumptions," Environmental Technology Letters 9: 479-490, 1988.

7. Uberla, K., "Epidemiology: Its Scope and Limitations for Indoor Air Quality." In: Indoor Air Quality: Symposium. Buenos Aires, National Academy of Sciences of Buenos Aires, 45-60, 1989.

8. Mantel, N., "Lung Cancer and Passive Smoking," British Medical Journal 294: 440, 1987.

9. Kabat, G. and Wynder, E., "Lung Cancer in Nonsmokers," Cancer 53(5): 1214-1221, 1984.

10. Garfinkel, L., Auerbach, O. and Joubert, L., "Involuntary Smoking and Lung Cancer: A Case-Control Study," Journal of the National Cancer Institute 75(3): 463-469, 1985.

2046157437

Source: https://www.industrydocuments.ucsf.edu/docs/qnwl0000

11. Wu, A., Henderson, B.E., Pike, M.C. and Yu, M.C., "Smoking and Other Risk Factors for Lung Cancer in Women," Journal of the National Cancer Institute 74(4): 747-751, 1985.

12. Janerich, D., Thompson, W.D., Varela, L.R., Greenwald, P., Chorost, S., Tucci, C., Zaman, M.B., Melamed, M.R., Kiely, M. and McKneally, M.F., "Lung Cancer and Exposure to Tobacco Smoke in the Household," New England Journal of Medicine 323: 632-636, 1990.

13. Kabat, G.C., "Epidemiologic Studies of the Relationship Between Passive Smoking and Lung Cancer." In: Toxicology Forum: 1990 Annual Winter Meeting. Washington, D.C., 187-199, February 19-21, 1990.

14. Fontham, E.T.H., Correa, P., Wu-Williams, A., Reynolds, P., Greenberg, R.S., Buffler, P.A., Chen, V.W., Boyd, P., Alterman, T., Austin, D.F., Liff, J. and Greenberg, S.D., "Lung Cancer in Nonsmoking Women: A Multicenter Case-Control Study," Cancer Epidemiology, Biomarkers & Prevention 1: 35-43, 1991.

15. Lee, P.N., Chamberlain, J. and Alderson, M.R., "Relationship of Passive Smoking to Risk of Lung Cancer and Other Smoking-Associated Diseases," British Journal of Cancer 54: 97-105, 1986.

16. Svensson, C., Pershagen, G. and Klominek, J., "Smoking and Passive Smoking in Relation to Lung Cancer in Women," Acta Oncologica 28(5): 623-639, 1989.

17. Kalandidi, A., Katsouyanni, K., Voropoulou, N., Bastas, G., Saracci, R. and Trichopoulos, D., "Passive Smoking and Diet in the Etiology of Lung Cancer Among Non-Smokers," Cancer Causes and Control 1: 15-21, 1990.

18. Koo, L.C., Ho, J.H.-C., Saw, D. and Ho, C.Y., "Measurements of Passive Smoking and Estimates of Lung Cancer Risk Among Non-Smoking Chinese Females," International Journal of Cancer 39: 162-169, 1987.

19. Shimizu, H., Morishita, M., Mizuno, K., Masuda, T., Ogura, Y., Santo, M., Nishimura, M., Kunishima, K., Karasawa, K., Nishiwaki, K., Yamamoto, M., Hisamichi, S. and Tominaga, S., "A Case-Control Study of Lung Cancer in Nonsmoking Women," Tohoku Journal of Experimental Medicine 154: 389-97, 1988.

2046157438

Source: https://www.industrydocuments.ucsf.edu/docs/qnwl0000

20. Wu-Williams, A.H., Dai, X.D., Blot, W., Xu, Z.Y., Sun, X.W., Xiao, H.P., Stone, B.J., Yu, S.F., Feng, Y.P., Ershow, A.G., Sun, J., Fraumeni, J.F and Henderson, B.E., "Lung Cancer Among Women in North-East China," British Journal of Cancer 62: 982-987, 1990.

21. Hirayama, T., "Non-Smoking Wives of Heavy Smokers Have a Higher Risk of Lung Cancer: A Study from Japan," British Medical Journal 282: 183-185, 1981.

22. Trichopoulos, D., Kalandidi, A., Sparros, L. and MacMahon, B., "Lung Cancer and Passive Smoking," International Journal of Cancer 27(1): 1-4, 1981.

23. Garfinkel, L., "Time Trends in Lung Cancer Mortality Among Nonsmokers and a Note on Passive Smoking," Journal of the National Cancer Institute 66(6): 1061-1066, 1981.

24. Chan, W.C. and Fung, S.C., "Lung Cancer in Non-Smokers in Hong Kong." In: Cancer Campaign Vol. 6, Cancer Epidemiology. E. Grundmann (ed.). Stuttgart, Gustav Fischer Verlag, 199-202, 1982.

25. Correa, P., Pickle, L.W., Fontham, E., Lin, Y. and Haenszel, W., "Passive Smoking and Lung Cancer," Lancet II: 595-597, 1983.

26. Buffler, P.A., Pickle, L.W., Mason, T.J. and Contant, C., "The Causes of Lung Cancer in Texas." In: Lung Cancer: Causes and Prevention. M. Mizell and P. Correa (eds.). Deerfield Beach, Verlag Chimie International, 83-99, 1984.

27. Gillis, C.R., Hole, D.J., Hawthorne, V.M. and Boyle, P., "The Effect of Environmental Tobacco Smoke in Two Urban Communities in the West of Scotland." In: ETS - Environmental Tobacco Smoke: Report from a Workshop on Effects and Exposure Levels. R. Rylander, Y. Peterson and M.-C. Snella (eds.). Published simultaneously in European Journal of Respiratory Disease, Supplement 133, Volume 65, 121-126, 1984.

28. Lam, W.K., A Clinical and Epidemiological Study of Carcinoma of Lung in Hong Kong, M.D. Thesis Submitted to the University of Hong Kong, 1985.

29. Akiba, S., Kato, H. and Blot, W.J., "Passive Smoking and Lung Cancer Among Japanese Women," Cancer Research 46: 4804-4807, 1986.

2046157439

Source: https://www.industrydocuments.ucsf.edu/docs/qnwl0000

30. Brownson, R.C., Reif, J.S., Keefe, T.J., Ferguson, S.W. and Pritzl, J.A., "Risk Factors for Adenocarcinoma of the Lung," American Journal of Epidemiology 125(1): 25-34, 1987.

31. Gao, Y.-T., Blot, W.J., Zheng, W., Ershow, A.G., Hsu, C.W., Levin, L.I., Zhang, R. and Fraumeni, J.F., "Lung Cancer Among Chinese Women," International Journal of Cancer 40: 604-609, 1987.

32. Humble, C.G., Samet, J.M. and Pathak, D.R., "Marriage to a Smoker and Lung Cancer Risk," American Journal of Public Health 77(5): 598-602, 1987.

33. Lam, T.H., Kung, I.T.M., Wong, C.M., Lam, W.K., Kleevens, J.W.L., Saw, D., Hsu, C., Seneviratne, S., Lam, S.Y., Lo, K.K. and Chan, W.C., "Smoking, Passive Smoking and Histological Types in Lung Cancer in Hong Kong Chinese Women," British Journal of Cancer 56(5): 673-678, 1987.

34. Pershagen, G., Hrubec, Z. and Svensson, C., "Passive Smoking and Lung Cancer in Swedish Women," American Journal of Epidemiology 125(1): 17-24, 1987.

35. Geng, G.-Y., Liang, T.H., Zhang, A.Y. and Wu, G.L., "On the Relationship Between Smoking and Female Lung Cancer." In: Smoking and Health 1987. M. Aoki, S. Hisamichi and S. Tominaga (eds.). Amsterdam, Excerpta Medica, 483-486, 1988.

36. Inoue, R. and Hirayama, T., "Passive Smoking and Lung Cancer in Women." In: Smoking and Health 1987. M. Aoki, S. Hisamichi and S. Tominaga (eds.). Amsterdam, Excerpta Medica, 283-285, 1988.

37. Sobue, T., Suzuki, R., Nakayama, N., Inubuse, C., Matsuda, M., Doi, O., Mori, T., Furuse, K., Fukuoka, M., Yasumitsu, T., Kuwabara, O., Ichigaya, M., Kurata, M., Kuwabara, M., Nakahara, K., Endo, S. and Hattori, S., "Passive Smoking Among Nonsmoking Women and the Relationship Between Indoor Air Pollution and Lung Cancer Incidence -- Results of a Multicenter Case Controlled Study," Gan to Rinsho 36(3): 329-333, 1990.

38. Liu, Z., He, X. and Chapman, R.S., "Smoking and Other Risk Factors for Lung Cancer in Xuanwei, China," International Journal of Epidemiology 20(1): 26-31, 1991.

39. Wynder, E.L. and Kabat, G.C., "Environmental Tobacco Smoke and Lung Cancer: A Critical Assessment." In: Indoor Air Quality. H. Kasuga (ed.). Berlin, Heidelberg, Springer-Verlag, 5-15, 1990.

2046157440

Source: https://www.industrydocuments.ucsf.edu/docs/qnwl0000

40. Gori, G.B. and Mantel, N., "Mainstream and Environmental Tobacco Smoke," Regulatory Toxicology and Pharmacology 14: 88-105, 1991.

41. Kilpatrick, S., "Misclassification of Environmental Tobacco Smoke Exposure: Its Potential Influence on Studies of Environmental Tobacco Smoke and Lung Cancer," Toxicology Letters 35: 163-168, 1987.

42. Friedman, G., Petitti, D.B. and Bawol, R.D., "Prevalence and Correlates of Passive Smoking," American Journal of Public Health 73(4): 401, 1983.

43. Pron, G.E., Burch, J.D., Howe, G.R. and Miller, A.B., "The Reliability of Passive Smoking Histories Reported in a Case-Control Study of Lung Cancer," American Journal of Epidemiology 127(2): 267-273, 1988.

44. Schenker, M., Hammond, K., Samuels, S., Kado, N. and Woskie, S., "Assessment of Environmental Tobacco Smoke Exposure in Epidemiologic Studies," Chest 91(2): 313-314, 1987. Abstract.

45. Lerchen, M.L. and Samet, J.M., "An Assessment of the Validity of Questionnaire Responses Provided by a Surviving Spouse," American Journal of Epidemiology 123(3): 481-489, 1986.

46. Sandler, D.P. and Shore, D.L., "Quality of Data on Parents' Smoking and Drinking Provided by Adult Offspring," American Journal of Epidemiology 124(5): 768-778, 1986.

47. Leaderer, B., "Assessing Exposures to Environmental Tobacco Smoke," Risk Analysis 10(1): 19-26, 1990.

48. Shimizu, Y., Namekata, T. and Takemoto, K., "Epidemiological Issues on Involuntary Smoking and Lung Cancer." In: Indoor Air Quality. H. Kasuga (ed.). Berlin, Heidelberg, Springer-Verlag, 323-332, 1990.

49. National Research Council, National Academy of Sciences, "Current and Anticipated Applications." In: Human Exposure Assessment for Airborne Pollutants: Advances and Opportunities. Washington, D.C., National Academy Press, 207-218, 1991.

50. Vaughan, W. and Hammond, K., "Impact of 'Designated Smoking Area' Policy on Nicotine Vapor and Particle Concentrations in a Modern Office Building," J Air Waste Manage Assoc 40: 1012-1017, 1990.

2046157441

Source: https://www.industrydocuments.ucsf.edu/docs/qnwl0000

51. Hedge, A., et al., "Building Ventilation and Smoking Policy Effects on Indoor Air Quality and Employee Comfort and Health." In: Indoor Air '90: Proceedings of the Fifth International Conference on Indoor Air Quality and Climate. Toronto, Canada, Volume 1, 739-744, July 29-August 3, 1990.

52. Sterling, T. and Mueller, B., "Concentrations of Nicotine, RSP, CO and CO_2 in Nonsmoking Areas of Offices Ventilated by Air Recirculated from Smoking Designated Areas," Am Ind Hyg Assoc J 49(9): 423-426, 1988.

53. Sterling, T., et al., "Exposure to Environmental Tobacco Smoke in the Non Industrial Workplace Under Different Conditions of Ventilation and Smoking Regulation." In: Present and Future of Indoor Air Quality. C.J. Bieva, et al. (eds.). Elsevier Science Publishers, Amsterdam, 111-118, 1989.

54. Malmfors, T., et al., "Air Quality in Passenger Cabins of DC-9 and MD-80 Aircraft," Environ Technol Letters 10: 613-628, 1989.

55. Oldaker, G., et al., "Estimation of Effect of Environmental Tobacco Smoke on Air Quality Within Passenger Cabins of Commercial Aircraft II." In: Indoor Air Quality and Ventilation, F. Lunau and G. Reynolds (eds.). London, Selper Ltd., 447-454, 1990.

56. Oldaker, G. and Conrad, F., "Estimation of the Effect of Environmental Tobacco Smoke on Air Quality Within Passenger Cabins of Commercial Aircraft," Environ Sci Technol 21: 994-999, 1987.

57. Sterling, T., "ETS Concentrations Under Different Conditions of Ventilation and Smoking Regulation." In: Indoor and Ambient Air Quality. R. Perry and P. Kirk (eds.). London, Selper Ltd., 89-98, 1988.

58. White, J. and Froeb, H., "Small-Airways Dysfunction in Nonsmokers Chronically Exposed to Tobacco Smoke," New England Journal of Medicine 302(13): 720-723, 1980.

59. Adlkofer, F., Scherer, G. and Weimann, H., "Small-Airways Dysfunction in Passive Smokers," New England Journal of Medicine 303(7): 392, 1980.

60. Huber, G., "Small-Airways Dysfunction in Passive Smokers," New England Journal of Medicine 303(7): 392, 1980.

61. Freedman, A., "Small-Airways Dysfunction in Passive Smokers," New England Journal of Medicine 303(7): 393, 1980.

2046157442

Source: https://www.industrydocuments.ucsf.edu/docs/qnwl0000

62. Aviado, D., "Small-Airways Dysfunction in Passive Smokers," New England Journal of Medicine 303(7): 393, 1980.

63. White, J. and Froeb, H., "Small-Airways Dysfunction in Passive Smokers," New England Journal of Medicine 303(7): 393-394, 1980.

64. Lebowitz, M., "Influence of Passive Smoking on Pulmonary Function: A Survey," Preventive Medicine 13(6): 645-655, 1984.

65. Kentner, M., Triebig, G. and Weltle, D., "The Influence of Passive Smoking on Pulmonary Function - A Study of 1,351 Office Workers," Preventive Medicine 13(6): 656-669, 1984.

66. Kentner, M. and Weltle, D., "Passive Tobacco Smoke Inhalation and Lung Function in Adults." In: Indoor and Ambient Air Quality. R. Perry and P. Kirk (eds.). London, Selper Ltd., 232-241, 1988.

67. Kentner, M., Weltle, D. and Valentin, H., "Passive Smoking and Lung Function in Adults," Arbeitsmedicine Sozialmedicine Praventivmedicine (24): 8-13, 1989.

68. Kentner, M. and Weltle, D., "Are There Any Impairments of Maximal Expiratory Flow-Volume Curves by Passive Smoking?" In: Indoor Air Quality. H. Kasuga (ed.). Berlin, Heidelberg, Springer-Verlag, 153-166, 1990.

69. Fielding, J.E. and Phenow, K.J., "Health Effects of Involuntary Smoking," The New England Journal of Medicine 319(22): 1452-1460, 1988.

70. Weiss, S.T., "What are the Health Effects of Passive Smoking?" The Journal of Respiratory Diseases 9(1): 46-48, 55, 58, 60, 62, 1988.

71. Weetman, D.F., and Munby, J., "Environmental Tobacco Smoke (ETS) and Cardiovascular Disease." In: Indoor Air Quality and Ventilation. F. Lunau and G.L. Reynolds (eds.). London, Selper Ltd., 211-216, 1990.

72. Thiery, J. and Cremer, P., "Coronary Heart Disease and Involuntary Smoking," The Toxicology Forum: 1990 European Meeting, Session on "Environmental Tobacco Smoke: Science and Meta-Science," Budapest, Hungary, June 19, 1990.

2046157443

Source: https://www.industrydocuments.ucsf.edu/docs/qnwl0000

73. Mahajan, V.K., and Huber, G.L., "Health Effects of Involuntary Smoking: Impact on Tobacco Use, Smoking Cessation, and Public Policies," Seminars in Respiratory Medicine 11(1): 87-114, 1990.

74. Armitage, A.K., "Environmental Tobacco Smoke and Coronary Heart Disease." In: Other People's Tobacco Smoke. A.K. Armitage (ed.). Beverly, East Yorks, United Kingdom, Galen Press, Chapter 7, 109-116, 1991.

75. Anonymous, "A Brief Summary of the Public Comments Submitted to the U.S. EPA in Response to the External Review Draft EPA/600/6-90/006A," submitted to the U.S. Environmental Protection Agency, Science Advisory Board Meeting, December 4-5, 1990.

76. Baker, R. and Proctor, C., "The Origins and Properties of Environmental Tobacco Smoke," Env Int 16: 231-245, 1990.

77. Lofroth, G., et al., "Characterization of Environmental Tobacco Smoke," Env Sci Technol 23: 610-614, 1989.

78. Reasor, M., and Will, J., "Assessing Exposure to Environmental Tobacco Smoke: Is It Valid to Extrapolate from Active Smoking?" Journal of Smoking Related Diseases 2(1): 111-127, 1991.

79. Proctor, C. and Dymond, H., "The Measurement of ETS Through Adsorption/Desorption Procedures." In: Indoor Air Quality. H. Kasuga (ed.). Berlin, Heidelberg, Springer-Verlag, 82-89, 1990.

80. Nystrom, C., et al., "Assessing the Impact of Environmental Tobacco Smoke on Indoor Air Quality: Current Status." In: Proceedings of the ASHRAE Conference, IAQ '86. Atlanta, Georgia, 213-233, April 20-23, 1986.

81. Scherer, G., et al., "Importance of Exposure to Gaseous and Particulate Phase Components of Tobacco Smoke in Active and Passive Smokers," Occup Env Health 62: 459-466, 1990.

82. Fleiss, J.L. and Gross, A.J., "Meta-Analysis in Epidemiology, with Special Reference to Studies of the Association Between Exposure to Environmental Tobacco Smoke and Lung Cancer: A Critique," Journal of Clinical Epidemiology 44(2): 127-139, 1991.

83. Letzel, H. and Uberla, K., "Meta-Analyses on Passive Smoking and Lung Cancer." In: Indoor Air Quality. H. Kasuga (ed.). Berlin, Heidelberg, Springer-Verlag, 316-322, 1990.

2046157444

Source: https://www.industrydocuments.ucsf.edu/docs/qnwl0000

84. Kirk, P., et al., "Environmental Tobacco Smoke in Indoor Air." In: Indoor and Ambient Air Quality. R. Perry and P. Kirk (eds.). London, Selper Ltd., 99-112, 1988.

85. Carson, J. and Erikson, C., "Results from Survey of Environmental Tobacco Smoke in Offices in Ottawa, Ontario," Environ Technol Letters 9: 501-508, 1988.

86. Sterling, T., et al., "Environmental Tobacco Smoke and Indoor Air Quality in Modern Office Work Environments," Journal of Occupational Medicine 26(1): 57-62, 1987.

87. Hosein, R., "The Relationship Between Pollutant Levels in Homes and Potential Sources." In: Indoor Air Quality in Cold Climates: Hazards and Abatement Measures. D. Walkinshaw (ed.). APCA, Ottawa, Ontario, 250-260, 1985.

88. Hinds, W. and First, M., "Concentrations of Nicotine and Tobacco Smoke in Public Places," New England Journal of Medicine 292(16): 844-845, 1975.

89. Badre, R., et al., "Pollution Atmospherique par la Fumee de Tabac (Atmospheric Pollution by Smoking)," Ann Pharm Fr 36(9-10): 443-452, 1978. Translation.

90. Jenkins, R., et al., "Development and Application of a Thermal Desorption-Based Method for the Determination of Nicotine in Indoor Environments." In: Indoor and Ambient Air Quality. R. Perry and P. Kirk (eds.). London, Selper Ltd., 557-566, 1988.

91. Muramatsu, M., et al., "Estimation of Personal Exposure to Tobacco Smoke with a Newly Developed Nicotine Personal Monitor," Environ Res 35: 218-227, 1984.

92. Muramatsu, M., et al., "Estimation of Personal Exposure to Ambient Nicotine in Daily Environment," Arch Occup Environ Health 59: 545-550, 1987.

93. Thompson, C., et al., "A Thermal Desorption Method for the Determination of Nicotine in Indoor Environments," Envir Sci Tech 23: 429-435, 1989.

94. Foliart, D., et al., "Passive Absorption of Nicotine in Airline Flight Attendants," New England Journal of Medicine 308(18): 1105, 1983.

2046157445

Source: https://www.industrydocuments.ucsf.edu/docs/qnwl0000

95. Letter to Dr. J. Donald Millar, Director, National Institute for Occupational Safety and Health, from Samuel D. Chilcote, Jr., President, The Tobacco Institute, August 1, 1991.

96. Repace, J. and Lowrey, A., "A Quantitative Estimate of Nonsmokers' Lung Cancer Risk from Passive Smoking," Environment International 11(1): 3-22, 1985.

97. Arundel, A., Sterling, T. and Weinkam, J., "Never Smoker Lung Cancer Risks from Exposure to Particulate Tobacco Smoke," Environment International 13: 409-426, 1987.

98. Lebowitz, M.D., "The Potential Association of Lung Cancer with Passive Smoking," Environment International 12: 3-9, 1986.

99. Johnson, C. and Letzel, H., "Letter to the Editors," Environment International 12: 21-22, 1986.

100. Burch, P.R.J., "Health Risks of Passive Smoking: Problems of Interpretation," Environment International 12: 23-28, 1986.

101. Kilpatrick, S.J., "Letter to the Editors," Environment International 12: 29-31, 1986.

102. Darby, S. and Pike, M., "Lung Cancer and Passive Smoking: Predicted Effects from a Mathematical Model for Cigarette Smoking and Lung Cancer," British Journal of Cancer 58: 825-831, 1988.

103. Gori, G. and Mantel, N., "Mainstream and Environmental Tobacco Smoke," Regulatory Toxicology and Pharmacology 14: 88-105, 1991.

104. McAughey, J., et al., "Respiratory Deposition of Environmental Tobacco Smoke." In: Indoor Air '90: Proceedings of the Fifth International Conference on Indoor Air Quality and Climate. Toronto, Canada, Volume 2, 361-366, July 29-August 3, 1990.

105. Bayard, S., Statement, The U.S. Environmental Protection Agency Science Advisory Board Hearing on Health Effects of Passive Smoking: Assessment of Lung Cancer in Adults and Respiratory Disorders in Children, External Review Draft, EPA/600/6-90/006A, 116-117, December 4, 1990. Transcript.

106. Wells, A.J., "An Estimate of Adult Mortality in the United States from Passive Smoking," Environment International 14(3): 249-265, 1988.

2046157446

Source: https://www.industrydocuments.ucsf.edu/docs/qnwl0000

107. Steenland, K., "Passive Smoking and the Risk of Heart Disease," JAMA 267(1): 94-99, 1992.

108. Glantz, S.A. and Parmley, W.W., "Passive Smoking and Heart Disease: Epidemiology, Physiology, and Biochemistry," Circulation 83(1): 1-12, 1991.

109. Helsing, K.J., Sandler, D.P., Comstock, G.W. and Chee, E., "Heart Disease Mortality in Nonsmokers Living with Smokers," American Journal of Epidemiology 127(5): 915-922, 1988.

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PHILIP MORRIS RESPONSE TO OSHA RFI

GLOSSARY

The attached glossary of scientific terms is provided for the reader's reference.

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GLOSSARY

Acute: Having a short course; of short duration.

Air conditioning: The process of treating air to meet the requirements of a conditioned space by controlling its temperature, humidity, cleanliness and distribution. (After ASHRAE 62-1989.)

Animal study: A controlled laboratory experiment in which animals are exposed to an agent and the biological effects of this exposure are assessed. The exposure may be via food or water (ingestion), by injection, by external application or by inhalation. Typical effects that might be measured are tumor incidence or tissue and organ changes.

Antigen: A substance capable of producing an immune response.

Atopy: A predisposition toward the development of allergies.

Bias: Nonrandom error. Regarding epidemiologic studies, the operation of factors in a study's design or execution that erroneously lead to the appearance of a stronger or weaker association between the agent in question and disease than in fact exists.

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Bioassay: The determination of the activity of a sample of an agent by noting its effect on a live animal or an isolated organ preparation.

Carcinogen: A substance or agent designated as capable of producing or initiating cancer.

Case-control study: A type of epidemiologic study which compares diseased persons (cases) with nondiseased persons (controls) in association with a common exposure to an agent. The previous exposures of both groups are investigated.

Chronic: Persisting over a long period of time. Regarding animal studies, refers to administration of the test substance over a period of several weeks or months.

Cohort study: An epidemiologic study which examines the development of a disease in a group (cohort) of persons who are currently free of the disease. May assess exposure either prospectively or retrospectively.

Confidence interval (CI) and confidence limits: The values between which a risk estimate may be expected to fall 95% of the time based on the variability of the underlying data. When the 95% confidence limits are both greater and less than 1.00

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(i.e., the confidence interval includes 1.00), the risk value is considered not statistically significant, i.e., the results are likely to be due to chance and do not support a judgment regarding an association between exposure and disease.

Confounding: As applied to epidemiologic studies, the situation in which the relationship between an agent and a disease appears stronger or weaker than it truly is due to the influence of another unknown or unrecognized factor. In confounding, the agent under consideration is associated with another agent (a confounding factor, or confounder) which is itself associated with either an increase or decrease in the incidence of the disease.

Dose-response assessment: Defines the relationship between the dose of an agent and the probability of induction of a carcinogenic effect.

Environmental tobacco smoke (ETS) [called "passive tobacco smoke" ("PTS") in the OSHA RFI]: Consists of smoke originating from the smoldering end of a tobacco product between puffs, e.g., sidestream smoke, and of smoke exhaled by the smoker. The components are released into the environment where they are diluted by ambient air and undergo changes related to aging over time.

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Epidemiology: The branch of science concerned with the patterns of disease in human populations and the various factors that influence these patterns.

Flow volume curve: A graphic analysis of the flow generated during an FEV maneuver plotted against volume change, followed by an FIV (forced inspiratory volume) maneuver plotted similarly.

Forced expiratory flow ($FEF_{25-75\%}$): The average rate of flow during the middle half of an FEV maneuver, recorded in liters per second or liters per minute.

Forced expiratory flow ($FEV_{1.0}$): The volume of gas expired over a given time interval (in this instance, one second) of an FVC maneuver.

Forced vital capacity (FVC): The maximum volume of gas that can be expired as forcefully and rapidly as possible after maximal inspiration, recorded in liters.

Gas: A state of matter in which substances exist in the form of nonaggregated molecules. (After ASHRAE 62-1989.)

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Hypersensitivity: A state of altered reactivity in which the body reacts with an exaggerated immune response to a foreign substance.

In vitro: Literally, within glass; used to refer to laboratory procedures conducted in a test tube or similar location, often involving preparations of cells or tissues.

In vivo: Literally, within the living body; used to refer to laboratory procedures utilizing live animals.

Mainstream smoke (MS): Tobacco smoke drawn through the butt end of a cigarette.

Maximum expiratory flow (MEF_{25-75}): The maximum amount of air that can be expelled from the lungs during the middle half of a maximum expiratory flow (MEF) procedure.

Meta-analysis: A statistical technique for combining studies into a single analysis, designed to increase the ability to statistically detect an association if such an association is present.

Microorganism: A microscopic organism, especially a bacterium, fungus or a protozoan. (After ASHRAE 62-1989.)

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Mutagen: An agent that tends to increase the frequency or extent of mutation, i.e., physical or biochemical changes in the genetic material of an organism.

Mutagenicity: The property of being able to induce genetic mutation.

Odds ratio: A measure of risk obtained from epidemiological studies and mathematically close to relative risk ("point estimate" or "risk estimate" may also be used to refer to this measure).

Odor: A quality of gases, liquids or particles that stimulates the olfactory organ. (After ASHRAE 62-1989.)

Particulate matter: A state of matter in which solid or liquid substances exist in the form of aggregated molecules or particles. (After ASHRAE 62-1989.)

Peak expiratory flow: The maximum flow rate attained at any time during an FEV maneuver, recorded in liters per second or liters per minute.

p-value: A statistical estimate of the probability that a finding is due to chance. By convention, a finding with a p-value less

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than 5% (i.e., 0.05), or sometimes 1%, is called statistically significant. A p-value less than 0.05 means that the observed results would occur by chance less than 5 times out of 100.

Relative risk: The ratio of the incidence rate of a disease among individuals exposed to a particular risk factor to the incidence rate among unexposed individuals.

Respirable particles: Ambient particles capable of penetrating into the nonciliated portion of the lung. Particles greater than 10 μm aerodynamic diameter are not respirable. (After ASHRAE 62-1989.) (One μm [micrometer or micron] equals 1/1,000,000 of a meter, or approximately 4/100,000 of an inch.)

Short-term tests: In vitro (performed on cells or tissue cultures) tests for mutations, including tests for chromosome aberrations, DNA damage/repair and other transformations which provide supportive evidence of cellular changes and may give information on carcinogenic mechanisms.

Sidestream smoke (SS): Smoke originating from the smoldering end of a tobacco product between puffs.

Standardized mortality ratio (SMR): A statistical comparison of the number of observed deaths in a study population and the

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number of expected deaths in a study population.

Statistical significance: A procedure to quantify the probability that an observed outcome, e.g., an association between an exposure and a disease endpoint, arose from random variation alone. The scientific community often uses 5% as a standard level at which data are accepted as occurring other than by chance. This means that there is a 95% probability that the results are not attributable to chance.

Syndrome: A set of symptoms which occur together.

Synergistic: Acting together; enhancing the effect of another force or agent.

Toxicology: The scientific study of the adverse effects of chemical or physical agents on biological systems.

Ventilation: The process of supplying and removing air by natural or mechanical means to and from any space. Such air may or may not be conditioned.

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PHILIP MORRIS RESPONSE TO OSHA RFI

Question 2a(i): "What data are available that associate adverse health effects with exposure to chemical agents?"

Summary:

There is a substantial body of scientific literature which suggests that exposure to various chemical agents in the indoor environment is associated with adverse health effects. Moreover, the literature suggests that exposure to chemical agents may be associated with symptoms of "sick building syndrome." Reported symptoms of exposure to chemical agents include headaches, dizziness, lung function impairment, fatigue, eye, nose and throat irritation, memory difficulties, and, possibly, decreased immunity. Some scientists have reported that there are possible synergistic reactions that occur between these different chemical agents in the indoor environment. Attempts to control individual sources of chemical agents in the indoor environment may not be sufficient to prevent the possible combined effects of the chemical agents. Therefore, in order to substantially reduce health complaints associated with exposure to chemical agents in the indoor air, adequate ventilation should be mandated in the workplace.

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PHILIP MORRIS RESPONSE TO OSHA RFI

Question 2a(i): "What data are available that associate adverse health effects with exposure to chemical agents?"

Response:

The available scientific literature on volatile organic compounds (VOCs) in the indoor environment suggests that exposure to VOCs may be associated with a variety of health effects. There are as many as 75 different VOCs that may be emitted by potential sources in the indoor environment.[1] The potential health effects of complex mixtures of these entities, and the possible synergistic reactions that may occur between them, have not been fully studied.

One study suggests that as many as 75 different VOCs may be emitted by potential sources in the indoor environment.[1] These VOCs can be sub-divided into nine different categories. The alkanes consist of n-hexane, n-heptane, n-octane, n-nonane, n-decane, n-undecane, n-dodecane, n-tridecane, n-tetradecane, n-pentadecane, n-hexadecane, 3-methylpentane, 2-methylhexane and 3-methylhexane. The cycloalkanes include cyclohexane, methylcyclohexane, and dimethylcyclopentane. Limonene, pinene, and terpinene comprise the terpene group.

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The aromatic compounds consist of benzene, toluene, m,p,xylene, o-xylene, ethylebenzene, n-propylbenzene, i-propylbenzene, 0-methylethylbenzene, 1,2,3 trimethylben, 1,2,4 trimethylben, 1,3,5 trimethylben, n-butylbenzene, p-methyl, isopropy, diethlbenzene, and styrene. Chloroform, dichloromethane, tetrachloromethane, bromoform, 1,2 dichlorethane, trichloroethane, 1,1,1 trichlorethane, trichlorethylene, tetrachloroethylene, chlorobenzene, m-dichlorobenzene, p-disclorobenzene, 1,2,3 trichloroben, 1,2,4 trichloroben, and 1,3,5 trichloroben are included in the chlorin compounds category.[1]

The alcohol group of VOCs consists of ethanol, propanol, n-butanol, i-butanol, pentanol, hexanol, and 2-ethylhexanol. Ethyl acetate, n-butyl acetate, ethylmethyl ketone, 4-meth.2-pentanone, hexanal, and nonanal are the carbonyl compounds. Other compounds include PAH, naphthalene, 1-methylnaphthalene, and Benzo-a-pyrene. The without classification group consists of formaldehyde, acetaldehyde, acrolein, butanal, nitrosamines, aromatic amines and acrylonitrile.[1]

According to the scientific literature available, these VOCs may be contributed by many potential sources in the indoor environment. A book on formaldehyde sensitivity and toxicity states that indoor sources of VOCs may include adhesives, glues, pastes, cements, carpet and toilet cleaners, cutting fluids, detergents,

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disinfectants/deodorants, dry cleaning fluids, dyes, inks, fur and leather, paints, lacquers, varnishes, anticorrosion paint, paint and varnish remover, paper, photography developers, stabilizers, and hardeners, polishes and finishes, room deodorizers, mildew preventives, pressed wood products, wax, and textiles.[2]

It has been suggested that PTS is a significant contributor to formaldehyde and benzene levels in the indoor environment. According to some authors, however, this is not the case.[3-5] Dr. Thad Godish, a researcher from Indiana, has reported that "tobacco smoke does not appear to increase vapor-phase formaldehyde levels significantly in indoor environments."[3] English researchers, Proctor, et al., have reported similar findings with total VOC levels in the indoor environment.[4] They wrote:

> ETS did not significantly contribute to levels of volatile organic compounds in office air. In direct conflict with the findings of the U.S. EPA TEAM study, our research suggests that tobacco smoking does not result in significant increases of compounds such as benzene in office air.

Aldokofer, et al., reported that "[a]lthough the data of Wallace (1989) indicate such a possibility, it remains doubtful whether an increased benzene concentration in blood or in exhaled air, as observed after an ETS exposure, can be found under real life conditions."[5] The authors also suggested that "benzene uptake under ETS conditions is neglectable on the background of the body burden

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caused by other environmental sources" and that "it is highly questionable whether it poses a health risk to the general population."

There is scientific literature that supports the claim that exposure to VOCs may be associated with adverse health effects. For example, a 1982 paper suggested the following regarding the alleged health risks of exposure to formaldehyde:[6]

> The recent ban of UFFI by the Consumer Product Safety Commission (CPSC), the report of formaldehyde induced nasal carcinogenesis in rats by the Chemical Industry Institute for Toxicology (CIIT) study, and evidence of formaldehyde hypersensitivity among individual members of the population serve to illustrate the concerns associated with exposure to formaldehyde in the indoor environment.

Another study reported that "short-term exposure" to formaldehyde produces symptoms including eye, nose, throat and skin irritation, but that "long exposures" to formaldehyde may alter the structure and function of the respiratory system and may cause chronic respiratory disease.[7] The authors wrote:

> Formaldehyde is a toxic chemical that illustrates problems of indoor air pollution: used in resins that are a part of many home products, including particle board, plywood and urea formaldehyde foam insulation, it causes adverse health effects when it 'offgasses' from these products into a tightly-sealed occupied building. Most noticeably,

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formaldehyde irritates eyes, skin, and respiratory tract and causes allergic reactions, but these may not be its most serious effects. Formaldehyde also causes mutagenic and carcinogenic changes in test animals, and may cause these effects in humans.

A 1990 article reported on health effects associated with low-level and high-level VOC exposures.[8] For low-level exposures, the article stated that the "responding tissues are mucousal membranes in eyes, nose and throat; skin in face, neck and hands; upper and lower airways." This study suggested a biological model of reactions to low-level VOC exposures: 1) perception of the environmental exposure caused by acute stimulations of senses; 2) perception or observation of acute or subacute inflammatory-like reactions mostly in the exposed tissues; and 3) a number of effects which may be classified as a group of subacute environmental stress reactions caused by the perceptions. The author concluded that the reported findings "indicate that VOCs may be important for the indoor air quality especially in the form of discomfort due to odors and irritative symptoms in eyes, nose, and throat, and headache" and that "the syndrome may include other effects related, for example, to productivity and performance" not yet positively identified.

The authors of another study assessed the neurobehavioral and sensory irritant effects of a complex VOC mixture in a normal, healthy population with no known sensitivity to chemicals.[9] They

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reported an increased incidence of symptoms characteristic of "sick building syndrome," although they did not report that VOC exposure resulted in impaired memory and sensorimotor performance.

In 1989, Thrasher, et al., reported on the possible development of antibodies (indicative of an immune response) to formaldehyde, toluene, and trimellitic anhydride in all full-time employees of redecorated offices.[10] Smoking was prohibited in the offices. All of the subjects reportedly had symptoms involving the central nervous system, such as headaches and difficulty with current memory, as well as chronic malaise and fatigue. Other complaints often reported included a flulike illness, muscle pain/spasm, nausea, sinusitis, dizziness, eye irritation, rhinitis, depression, joint pain, sore throat, wheeze and cough, irritability, diarrhea and constipation, and altered olfaction.

The authors concluded that "[s]ince HCHO [formaldehyde], TDI [toluene], and TMA [trimellitic anhydride] are constituents of building materials and since antibodies to albumin conjugates have been associated with illness," immunological mechanisms may explain the existence of hypersensitivity pneumonitis, allergic rhinitis, asthma, and skin eruptions that have been reported in cases of tight building syndrome. These authors had previously reported that formaldehyde exposure appeared to be associated with a chronic antigenic stimulation of the immune system in six patients.[11]

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In a study of formaldehyde levels in mobile homes, a group of investigators reportedly observed a synergistic effect between formaldehyde exposure and chronic respiratory and allergy problems.[12] They also observed a positive exposure-response association for burning/tearing eyes over the exposure ranges studied.

In a study of exposure to 22 volatile organic compounds in the indoor air environment in 62 human subjects for 2.75 hours, Molhave, et al., reported that there was a significant effect of exposure to VOCs on responses to questions about general air quality, odor, ability to concentrate, and mucous membrane irritation.[13] The effect on eye, nose and throat irritation was acute and showed no signs of adaptation. The effects were significantly correlated with exposure both at 5 and 25 mg/m^3.

Molhave, in another 1986 paper, suggested that there is possibly a "sub-syndrome" which relates mucous membrane irritation-sensory irritation, dryness in nose and eye, which are very frequent symptoms with "sick building syndrome," to the total concentration of VOCs.[14] However, the author claims that the proposed dose-response relation is multifactorial, meaning that the reported response may also depend on such factors as ventilation rate, relative humidity and temperature.

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In a report of 100 structures investigated by the Wisconsin Division of Health from January, 1978 to November, 1979, occupants complained of eye irritation, burning eyes, runny nose, dry or sore throat, headache, and cough.[15] The authors reported that the "[o]bservations presented suggested nonoccupational, indoor environmental exposure to formaldehyde is significant and may reach levels which exceed occupational exposure standards." Another study reported the following regarding the literature on VOC exposure and associated health parameters:[16]

> The perception of occupants with respect to both poor air quality and odor intensity increased with the total VOC concentration. Perception of dry mucous membranes was equally high at both 5 and 25 mg/m^3, and much higher than with clean air, consistent with the existence of a threshold. In summary, there are now results from controlled experiments that associate some of the symptoms reported by occupants of complaint buildings with exposure to VOCs at concentrations well below occupational standards but which are consistent with concentrations found in nonindustrial indoor air.

Hal Levin & Associates wrote the following regarding the alleged health effects of exposure to VOCs in the indoor air environment:[17]

> The health effects of most VOCs emitted from building materials are not well understood, but many are known or suspected human irritants

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and carcinogens. In one study, Lars Molhave of Denmark found that 82% of commonly emitted VOCs are known or suspected mucous membrane or eye irritants, and 25% are known or suspected human carcinogens.

In a 1989 study of formaldehyde exposure and its possible acute health effects, a group of investigators reported that "there was a significant relationship between HCHO [formaldehyde] exposure and variability in peak expiratory flows that was dependent on age group" and that "[i]t may be especially important to assess the variability in reactive individuals and children to determine the short-term effects of HCHO exposures and possible long-term consequences."[18]

In 1982, one investigator suggested that "the possibility of negative health effects [of organic gases and vapours of solvents in building materials] cannot be neglected, especially not for the more sensitive minority of the general population."[19]

Researchers have suggested that "some office workers may be constantly exposed to measurable formaldehyde concentrations as a result of offgassing from particleboard used in furniture and wall coverings."[20] These researchers have reported that "workers in industry and professionals exposed to formaldehyde show a higher than expected SMR for almost all types of cancer, but especially for cancer of the brain." However, the authors acknowledged that

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indoor formaldehyde exposures may sometimes be too short to constitute a significant cancer risk. The authors suggested that "reliance on regulations concerning specific substances may be insufficient" and that "insistence upon adequate ventilation appears as a universally more useful strategy." They recommended that standards are established and enforced to ensure more adequate ventilation. The authors claimed that "an increase in ventilation rates would not only reduce indoor concentrations of widespread carcinogens such as radon daughters and combustion byproducts but also reduce discomfort and a variety of chronic indoor health problems such as allergies, respiratory infections and headaches."

Another group of researchers has stated that "[i]t seems reasonable to view formaldehyde as though it were a carcinogen for humans," but "[t]he central question is how much of a carcinogenic risk does low-level exposure to formaldehyde pose under realistic environmental conditions?"[21]

In a case history of a five-level office building, two researchers reported that the occupants of the building had experienced multiple adverse health symptoms, and it was believed that poor indoor air quality was the culprit.[22] A pollutant survey of the building revealed the presence of a large number of airborne volatile organic compounds. The primary source of the VOCs, and an irritating odor, was identified as a chemical deodorizer being

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used in the building and its air handling room. The authors concluded that "inadequate ventilation and high levels of complex mixtures of VOCs appeared to be the primary problems associated with the building."

At least two research groups have studied the possible relationship between formaldehyde particles and asthma.[23,24] One of these research groups reported that "the breathing zone concentrations of formaldehyde required to elicit these irritant reactions (mean 4.8 mg/m^3) were higher than those encountered in buildings recently insulated with urea formaldehyde foam, but within levels sometimes found in industry."[23] The authors concluded that "the results show that formaldehyde exposure can cause asthmatic reactions, and suggest that these are sometimes due to hypersensitivity and sometimes to a direct irritant effect."

Researchers who studied the possible acute respiratory effects of low-level exposure to formaldehyde and sulfur dioxide reported that "[i]n general the number and severity of complaints increased with SO_2 dose in both healthy and asthmatic subjects." Asthmatics complained of progressive lower airway symptoms, while healthy subjects complained more of upper respiratory symptoms. Regarding formaldehyde, the authors reported that low-level formaldehyde exposure did not appear to affect lung function in

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healthy or asthmatic subjects, while there were complaints of odor, sore throat, nasal discharge, stuffiness and eye irritation.[25]

Levin and Purdom reported in 1983 that "[s]ome of the health problems associated with building materials are created or increased when building heat losses and, consequently, the general ventilation of interior spaces are reduced." The authors go on to discuss exposure to formaldehyde gas from its release from urea-formaldehyde foam, including particular regulation activity in several states.[26]

Researchers in Denmark have reported that "even small concentrations of the relatively inert n-decane caused symptoms similar to those indicated in the World Health Organization definition of the sick building syndrome."[27] N-decane, like other VOCs, is reportedly released from building materials in the indoor environment.

Recently, at least one group of researchers has emphasized that the total VOC level in a given indoor environment constitutes a complex mixture of many different compounds.[28] Although many of the compounds might not be found in significant amounts in indoor air, researchers have not fully studied the possible additive or synergistic effects that may occur between low levels of various volatile organic compounds in the indoor environment. Therefore,

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VOCs might best be controlled as a mixture of individual compounds that might have undetermined synergistic effects on the health of occupants of inadequately ventilated workplaces.

Carbon Monoxide

There are several suggestions in the literature that underground parking garages in high rise buildings may contribute levels of carbon monoxide to the indoor office environment.[29-30] Reportedly, the CO from the parking garages enter the interior of the building via elevator shafts and stairwells. The authors stated that in buildings with elevated CO, the "occupants of such buildings simply may be unaware of their indoor CO problems, and they may attribute their symptoms -- such as headaches and dizziness -- to other causes."[30] Another study indicated that underground offices with parking garages on the same level are vulnerable to indoor air quality problems because of elevated CO levels.[31] Some high-rise buildings may also have restaurants at a lower level that use gas-stoves for cooking and contribute CO to the indoor environment.[30]

Nitrogen Dioxide

Investigators from the Health Effects Institute at the University of Rochester have reported on the possible adverse health

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effects of exposure to nitrogen dioxide.[32] They wrote the following:

> In summary, low-level continuous exposure to nitrogen dioxide caused a slight increase in airway reactivity, in agreement with other recent studies. Collectively, this study and prior studies provide some evidence that alveolar macrophages obtained by bronchoalveolar lavage 3.5 hours after exposure to nitrogen dioxide might inactivate influenza virus in vitro less effectively than do cells collected after air exposure.

They stated that although the status of NO_2 as a contaminant affecting the public health is uncertain, "[o]n the basis of epidemiological studies of air pollution, a plausible association between NO_2 levels and adverse health effects has been established." They also report that a few animal studies have suggested that NO_2 impairs antiviral defenses. Although the HEI research revealed few definitive conclusions, the authors suggest that "efforts to characterize the influence of NO_2 inhalation, including repeated exposures, on respiratory defense mechanisms are warranted if a more scientifically credible data base is desired for the standard-setting process."

A 1987 study reported that gaseous substances such as nitrogen dioxide stimulate the transformation of polycyclic aromatic hydrocarbons and that "the transformation products display a broad spectrum of mutagenicity, genotoxicity, and

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carcinogenicity."[33] They conclude that "indoor pollutants that are emitted from kerosene heaters, gas burners, and liquefied-petroleum burners contain numerous nitroarenes possessing potential mutagenicity, as reported previously."

Recently, researchers reported that there is a possible association between nitrogen dioxide exposure and the occurrence of influenza. They stated that "our findings suggest, but do not prove, that NO_2 alone may play a role in increasing susceptibility of adults to respiratory virus infections."[34] Other authors have reported the following regarding nitrogen dioxide exposure:

> These toxicological data suggest that exposure to NO_2 might adversely affect lung function, increase respiratory symptoms, exacerbate the status of persons with preexisting lung conditions such as asthma and chronic obstructive pulmonary disease, and increase rates of respiratory infection.[35]

Carbon Dioxide

Researchers from the United States Airforce have reported that "the symptoms of fatigue, drowsiness, feeling of temperature extremes, dizziness, increased ear, nose and throat problems are correlated with increased CO_2 and decreased humidity" and that "our analysis also indicates a tendency for increased headaches and problems breathing with increased CO_2 and decreased RH [relative

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humidity]."[36] Carbon dioxide is reportedly contributed by combustion sources in the indoor environment. They also reported that "the foregoing information demonstrates that, with increasing CO_2 levels there are increasing complaints, increased rates of respiratory illness, and loss of productivity which more than offsets energy savings" and that "studies on the physical and psychological effects of inadequate ventilation show clearly that noticeable [sic] effects occur at very low levels of CO_2."

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REFERENCES

1. Stolwijk, J.A.J., "Workshop on Indoor Air Quality: Assessment of Population Exposure and Carcinogenic Risk Posed by Volatile Organic Compounds in Indoor Air," Risk Analysis 10(1): 49-57, 1990.

2. Feinman, S.E., "Chapter 2: Exposure to Formaldehyde," In: Formaldehyde Sensitivity and Toxicity. CRC Press: Boca Raton, Florida. pp. 17-36, 1988.

3. Godish, T., "Formaldehyde Exposures from Tobacco Smoke: A Review," American Journal of Public Health 79(8): 1044-1045, 1989.

4. Proctor, C.J., Warren, N.D. and Bevan, M.A.J., "Measurements of Environmental Tobacco Smoke in an Air-Conditioned Office Building," Environmental Technology 10: 1003-1018, 1989.

5. Aldokofer, F., Scherer, G., Conze, C., Angerer, J. and Lehnert, G., "Significance of Exposure to Benzene and Other Toxic Compounds Through Environmental Tobacco Smoke," Journal of Cancer Research and Clinical Oncology 116: 591-598, 1990.

6. Hawthorne, A.R. and Gammage, R.B., "Formaldehyde Release from Simulated Wall Panels Insulated with Urea-Formaldehyde Foam Insulation," Journal of the Air Pollution Control Association 32(11): 1126-1131, 1982.

7. Beall, J.R. and Ulsamer, A.G., "Toxicity of Volatile Organic Compounds Present Indoors," Bulletin of the New York Academy of Medicine 57(10): 978-996, 1981.

8. Molhave, L., "Volatile Organic Compounds, Indoor Air Quality and Health," Indoor Air '90 5: 15-33, 1990.

9. Otto, D., Molhave, L., Rose, G., Hudnell, H.K. and House, D., "Neurobehavioral and Sensory Irritant Effects of Controlled Exposure to a Complex Mixture of Volatile Organic Compounds," Neurotoxicology and Teratology 12: 649-652, 1990.

10. Thrasher, J.D., Madison, R., Broughton, A. and Gard, Z., "Building-Related Illness and Antibodies to Albumin Conjugates of Formaldehyde, Toluene Diisocyanate, and Trimellitic Anhydride," American Journal of Industrial Medicine 15: 187-195, 1989.

11. Thrasher, J.D., Broughton, A. and Micevich, P., "Antibodies and Immune Profiles of Individuals Occupationally Exposed to

2046157479

Source: https://www.industrydocuments.ucsf.edu/docs/qnwl0000

Formaldehyde: Six Case Reports," American Journal of Industrial Medicine 14: 479-488, 1988.

12. Liu, K.S., Huang, F.Y., Hayward, S.B., Wesolowski, J. and Sexton, K., "Irritant Effects of Formaldehyde Exposure in Mobile Homes," Environmental Health Perspectives 94: 91-94, 1991.

13. Molhave, L., Bach, B. and Pedersen, O.F., "Human Reactions to Low Concentrations of Volatile Organic Compounds," Environment International 12: 167-175, 1986.

14. Molhave, L., "Indoor Air Quality in Relation to Sensory Irritation Due to Volatile Organic Compounds," ASHRAE Transactions 92(1): 306-316, 1986.

15. Dally, K.A., Hanrahan, L.P. and Woodbury, M.A., "Formaldehyde Exposure in Nonoccupational Environments," Archives of Environmental Health 36(6): 277-284, 1981.

16. Girman, J.R., "Volatile Organic Compounds and Building Bake-Out," Occupational Medicine: State of the Art Reviews 4(4): 695-712, 1989.

17. Levin, H., "Building Materials and Indoor Air Quality," Occupational Medicine: State of the Art Reviews 4(4): 667-693, 1989.

18. Quackenboss, J.J., Lebowitz, M.D., Michaud, J.P. and Bronnimann, D., "Formaldehyde Exposure and Acute Health Effects Study," Environment International 15: 169-176, 1989.

19. Molhave, L., "Indoor Air Pollution Due to Organic Gases and Vapours of Solvents in Building Materials," Environment International 8: 117-127, 1982.

20. Sterling, T.D. and Arundel, A., "Possible Carcinogenic Components of Indoor Air: Combustion Byproducts, Formaldehyde, Mineral Fibers, Radiation, and Tobacco Smoke," Journal of Environmental Science and Health Part C. Environmental Health Sciences 2(2): 185-230, 1984.

21. Nelson, N., Levine, R.J., Albert, R.E., Blair, A.E., Griesemer, R.A., Landrigan, P.J., Stayner, L.T. and Swenberg, J.A., "Contribution of Formaldehyde to Respiratory Cancer," Environmental Health Perspectives 70: 23-35, 1986.

22. Black, M.S., Bayer, C.W. and Brackett, H.L., "An Office Building IAQ Problem Involving Volatile Organic Compounds," In: Practical Control of Indoor Air Problems. Proceedings

2046157477

Source: https://www.industrydocuments.ucsf.edu/docs/qnwl0000

of the ASHRAE Conference IAQ 87, May 18-20, 1987. Arlington, Virginia; Atlanta, Georgia. American Society of Heating Refrigerating, and Air-Conditioning Engineers, Inc., 72-87, 1987.

23. Burge, P.S., Harries, M.G., Lam, W.K., O'Brien, I.M. and Patchett, P.A., "Occupational Asthma Due to Formaldehyde," Thorax 40(4): 255-260, 1985.

24. Frigas, E., Filley, W.V. and Reed, C.E., "UFFI Dust. Nonspecific Irritant Only?" Chest 82: 511-512, 1982.

25. Witek, T.J., Schachter, E.N., Tosun, T., Leaderer, B.P. and Beck, G.J., "Controlled Human Studies on the Pulmonary Effects of Indoor Air Pollution: Experiences with Sulfur Dioxide and Formaldehyde," Environment International 12(1/4): 129-135, 1986.

26. Levin, L. and Purdom, W.P., "A Review of the Health Effects of Energy Conserving Materials," American Journal of Public Health 73(6): 683-690, 1983.

27. Kjaergaard, S., Molhave, L. and Pedersen, O.F., "Human Reactions to Indoor Air Pollutants: n-Decane," Environment International 15: 473-482, 1989.

28. Feron, V.J., Til, H.P., de Vrijer, F. and van Bladeren, P.J., "Toxicology of Volatile Organic Compounds in Indoor Air and Strategy for Further Research," Indoor Environment 1: 69-81, 1992.

29. Grot, R.A., Hodgson, A.T., Daisey, J.M. and Persily, A., "Indoor Air Quality Evaluation of a New Office Building," ASHRAE Journal 33(9): 16-25, 1991.

30. Flachsbart, P.G. and Ott, W.R., "A Rapid Method for Surveying CO Concentrations in High-Rise Buildings," Environment International 12: 255-264, 1986.

31. Wallace, L., "Carbon Monoxide in Air and Breath of Employees in an Underground Office," Journal of the Air Pollution Control Association 33(7): 678-682, 1983.

32. Utell, M.J., Frampton, M.W., Roberts, N.J., Finkelstein, J.N., Cox, C. and Morrow, P.E., "Mechanisms of Nitrogen Dioxide Toxicity in Humans," Health Effects Institute Report No. 43: 1-44, 1991.

33. Tokiwa, H., Nakagawa, R., Horikawa, K. and Ohkubo, A., "The Nature of the Mutagenicity and Carcinogenicity of Nitrated,

2046157478

Source: https://www.industrydocuments.ucsf.edu/docs/qnwl0000

Aromatic Compounds in the Environment," Environmental Health Perspectives 73: 191-199, 1987.

34. Goings, S.A.J., Kulle, T.J., Bascom, R., Sauder, L.R., Green, D.J., Hebel, J.R. and Clements, M.L., "Effect of Nitrogen Dioxide Exposure on Susceptibility of Influenza A Virus Infection in Healthy Adults," American Review of Respiratory Disease 139(5): 1075-1081, 1989.

35. Lambert, W.E. and Samet, J.M., "The Role of Combustion Products in Building-Associated Illness," Occupational Medicine: State of the Art Reviews 4(4): 723-733, 1989.

36. Carpenter, D. and Poitrast, B.J., "Recommended Carbon Dioxide and Relative Humidity Levels for Maintaining Acceptable Indoor Air Quality," Air Force Occupational and Environmental Health Laboratory, Human Systems Division, AFOEHL Report 90-169CA00111KGA, 1-30, 1990.

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PHILIP MORRIS RESPONSE TO OSHA RFI

Question 2a(ii): "What data are available that associate adverse health effects with exposure to bioaerosols?"

Summary:

Bioaerosols, i.e., biological agents such as viruses, bacteria, fungi and their products, have been linked to a number of diseases and conditions. Such illnesses include Legionnaires' disease, hypersensitivity pneumonitis, humidifier fever, asthma, sick building syndrome and cold or influenza. The incidence of many of these illnesses has been linked to improper maintenance of ventilation systems or to inadequate levels of air exchange. For instance, the organism responsible for Legionnaires' disease, a form of severe, sometimes fatal, pneumonia, has been isolated from water in ventilation systems. Humidifiers have been implicated in the development of hypersensitivity pneumonitis, a condition that may lead to permanent lung damage. Humidifier fever, asthma and sick building syndrome are less well-understood; however, these complaints may affect worker performance. Infectious diseases (e.g., cold or influenza) are also likely to be transmitted more readily in poorly ventilated buildings.

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PHILIP MORRIS RESPONSE TO OSHA RFI

Question 2a(ii): "What data are available that associate adverse health effects with exposure to bioaerosols?"

Response:

In 1984, the New York Academy of Medicine drafted a resolution on indoor air pollution, in which they stated:[1]

> By far the most important substances in indoor air that affect human health are infectious agents, primarily viruses and bacteria, in the form of aerosols or as a part of droplets or particles. These cause more than 60,000 deaths and 250 million disabling illnesses in the United States each year. Their effects upon health are many times greater than that of all other indoor air pollutants.

Recently, bioaerosols and their impacts on human health were described by Harriet Burge in a review article.[2] She wrote:

> [B]ioaerosols include vegetative microbial cells, their reproductive units, and metabolites that are small enough or sufficiently volatile to achieve aerial dispersion. Categories include viruses, bacteria, fungi, algae, and protozoa and their products. Most bioaerosols can probably act as sensitizing agents in susceptible hosts, whereas some cause infectious disease, and other bioaerosols produce toxins with both acute and chronic health effects.

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(Others have included rickettsiae and chlamydiae in the list of organisms as well.)[3]

The health effects that have been attributed to bioaerosols may be divided into two broad categories, as Philip Morey did in a 1988 article:[4]

> Microbial contaminants in the indoor environment may cause illness of two general types, namely, those that are infective and those that are allergic in nature. Legionella pneumophila may be infective in that it causes legionellosis among susceptible persons. In this illness the microorganism invades or colonizes an organ such as the lung. Allergic respiratory diseases, on the other hand, are caused by a hypersensitivity response to inhaled particles containing viable microorganisms. . . . These illnesses usually occur as a response to microbial antigens aerosolized from heating, ventilation, and air-conditioning (HVAC) system such as humidifiers or air washers which may be contaminated or from other building components that may have been damaged by recurrent floods or moisture.

Following are brief descriptions of particular diseases and conditions attributed in the scientific literature to bioaerosols. Included for each disease/condition are a discussion of its symptoms, the organism(s) known or thought to be responsible, and the components of heating, ventilating and air-conditioning (HVAC) systems thought to be involved in its transmission or development.

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Legionellosis

The bacterium Legionella pneumophila has been linked to two distinct, but related, illnesses: Legionnaires' disease, a multi-system disease including pneumonia, and Pontiac fever, a self-limited, flu-like illness characterized by fever, headache and muscle ache.[5] Airborne transmission of these diseases has been "firmly established."[5]

Legionella species may be ubiquitous in water systems; their growth is favored with temperatures between 37.7°C and 48.8°C.[6] Suitably warm and stagnant water may be found in ventilation system components, such as cooling towers (and other wet type heat rejection systems), evaporative condensers, humidifiers, potable water heaters and holding tanks, pipes, and faucet aerators.[7,8] It is believed that legionellae can survive the water treatment process that produces drinking water.[7] Treated drinking water may carry the bacteria to buildings where the bacteria can colonize plumbing fixtures, especially the service hot water system and the ventilation system. Heating, ventilation, and air-conditioning (HVAC) systems, particularly cooling towers and other water evaporation systems, may be colonized by Legionella if contaminated potable water is used as a source for their make-up water. This is possibly the most likely way that HVAC systems

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become contaminated with legionellae.[7]

If water in the cooling towers of a building's HVAC system is contaminated, the aerosol mist generated from that water is, of course, contaminated as well. This Legionella-contaminated mist, or aerosol, may then spread into other buildings through open windows and ventilation system air intakes. Legionellae can survive in the air long enough to still be virulent if the bacteria are inhaled by humans.[9]

Legionnaires' Disease is a form of severe pneumonia attributed to infection with Legionella via inhalation. Symptoms of Legionnaires' disease include high fever, chills, headaches, muscular aches and pains, dry coughs, chest pains, shortness of breath, mental confusion, abdominal pain, vomiting and diarrhea. Although abdominal pain, vomiting and diarrhea are symptoms of the disease, currently available data do not suggest that Legionnaires' disease is acquired by drinking contaminated water.[7] The abdominal symptoms may be produced by toxic substances released from bacteria in the lungs or other organs, e.g., the liver. Legionnaires' disease progresses quickly; initial symptoms (e.g., mild headache and cough) may worsen substantially within 24 hours, when body temperatures may rise to 104°F or higher.

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Case reports indicate that Legionnaires' disease may principally affect elderly men, especially immunocompromised individuals, i.e., persons whose defenses against infection are impaired, as by existing disease.[5,10] Winn proposes that a combination of risk factors would produce the highest probability of infection, e.g., decreased host defenses and exposure to an environmental source of virulent bacteria.[11] However, at least one study reported that, in a Legionnaires' disease outbreak in a British police headquarters building, the affected individuals were "relatively young" and only one was immunocompromised.[12] The recent outbreak in a California Social Security Administration building also apparently affected young (working-age) persons; nine cases were reported, with one fatality.[13]

Bardana reports that the attack rate varies between 1-7%, with a case fatality rate of about 15%.[14] Approximately 15% of individuals exposed to Legionella-contaminated aerosols contract Legionnaires' disease within 3-9 days of exposure.[7] The CDC estimates that 10,000 to 50,000 cases of Legionnaires' disease occur annually in the United States. Approximately 15% to 20% of those 10,000 to 50,000 patients may die from the disease.[9,15] Burge and Hodgson report that Legionella is "a major contributor to mortality in the U.S.: an estimated 5,000 to 7,000 deaths per year."[15]

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Pontiac fever, the other illness caused by Legionella, is marked by flu-like symptoms. Morey and Feeley note that some believe that, since Legionella has never been cultured from individuals with Pontiac fever, this illness represents an allergic reaction to air contaminated with Legionella rather than a true infection.[3] Pontiac fever often affects working-age adults; symptoms usually subside in approximately 48 hours, without antibiotic therapy or hospitalization. Attack rates are much higher with Pontiac fever, reaching as much as 95% of the exposed population.

Approximately 1,300 cases of legionellosis (Legionnaires' disease and Pontiac fever) were reported to the CDC in 1990 as occurring in the United States.[9] It has been suggested that the actual number of cases is much higher. Estimates of disease incidence of legionellosis have ranged from 25,000 to more than 100,000 cases per year.[9]

Hypersensitivity Pneumonitis

Hypersensitivity pneumonitis, (HP; also called extrinsic allergic alveolitis) is an inhalant-induced, immunologically-mediated inflammation of the alveoli (where air exchange occurs in the lung) and the bronchioles (the smallest conducting airways).[16] It has been suggested that HP develops following prolonged repeated

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and intense inhalation exposure to antigen (a substance capable of producing an immune response).[17]

Clinically, HP is characterized by intermittent chills, fever, dry cough and shortness of breath.[18] Chest x-rays show restrictions in lung function, gas transfer defects and nodular shadowing.[19] HP may resolve within hours or days, or, in more severe cases, may require weeks of convalescence. In the long-term, HP may lead to an accelerated decline in pulmonary function. While complete resolution often occurs, irreversible lung scarring and alveolar loss may follow intense, recurrent or prolonged exposure.[16] However, continual low-level antigen exposure may also lead to permanent lung damage, with large areas of tissue destruction.

HP is often diagnosed in individuals with workplace exposure; it is characteristic of this condition that symptoms subside when the affected individual is not at work.[19] Attack rates reportedly range from 1-71% of exposed populations,[14] and are generally higher among nonsmokers.[16]

The antigen responsible for HP has not been isolated, but heat-tolerant (thermophilic) organisms have been implicated. These include the dry-spored fungi (Aspergillus, Penicillium)[18] and the thermophilic actinomycetes (Micropolyspora,

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Thermoactinomyces).[17,19] Responses to these organisms have been confirmed by precipitating antibody tests. Bacterial endotoxin (a toxic substance associated with the outer cell membranes) has also been implicated. Heat-tolerant organisms may contaminate humidifiers and air-conditioning systems, particularly water reservoirs in the central ventilation system;[20] such contamination results in a continuing exposure to the antigen.

Humidifier Fever

Humidifier fever is a flu-like condition of variable severity, marked by fever, shivering, muscle and joint pains, malaise, headache, lethargy and shortness of breath.[19] There is some indication that lung function changes may occur. Burge has suggested that humidifier fever may be an early, transient phase of hypersensitivity pneumonitis.[20] Unlike HP, however, humidifier fever symptoms disappear with continued exposure and then reappear when the individual returns after a break from work.[19]

Inhalation challenge and antibody precipitation tests reveal that some antigen is related to the development of humidifier fever, possibly the same antigen exposure as HP.[19] Although the exact antigen is unknown (endotoxin has been proposed), molds, algae, and non-pathogenic bacteria have been found in contaminated humidifiers.

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Asthma

Asthma is characterized by variable bronchial narrowing, swelling of the airway lining and overproduction of viscid mucus.[16] Such events follow the reaction of allergens with allergen-specific immunoglobulin E (IgE) molecules in the respiratory tract.

Asthma is exacerbated by continued exposures to ambient levels of allergens.[19] Some case reports suggests that asthma attacks have been provoked by contaminated humidifiers in the home and workplace. In fact, one author wrote that[16]

> The most obvious associations between indoor fungal prevalence and induction of asthma have been observed during finite exposures associated with operation of humidifying devices.

A variety of microorganisms suspected of being associated with asthma have been located in humidifiers, but the causative agent is unknown.

Sick Building Syndrome (SBS)

Sick building syndrome is marked by such symptoms as headache, eye and throat irritation, nausea, dizziness, and fatigue. Several authors have proposed various biological contaminants as

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being related to the development of this syndrome. These include volatile organic compounds released by fungi, toxic agents and irritants like endotoxin (a bacterial product), and microbial and dust levels.

Burge has proposed that endotoxin released from humidifier reservoirs is related to building-related illness.[20] Bardana, et al., describe building-related illness as[14]

> an illness in which worker complaints of ill health in a particular building are more common than might be reasonably expected. . . . Most documented buildings represent tight, energy-efficient designs with mechanical rather than natural mechanisms of air exchange. Attack rates vary considerably and can approach 80% of building occupants. Common complaints include headache, ill-defined fatigue, and mucous membrane irritation of the respiratory passages.

Rylander and colleagues measured endotoxin and glucan (a fungal cell wall component) in a study of several residences in Sweden.[21] They reported apparent correlations between the amount of glucan and nasal irritation and hoarseness, and between the amount of endotoxin and cough and itchy eyes. Both substances have been identified in dusts collected in occupational settings, suggesting that these compounds may be related to SBS symptoms.

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In their study of a British Legionnaires' disease outbreak, O'Mahony and colleagues noted a correlation between the presence of Legionella and reported sick building syndrome symptoms.[12] They wrote:

> It is . . . possible that microorganisms could be one of the causes of the symptoms of the sick-building syndrome because, as in this building, an inadequately maintained cooling tower and air-conditioning system would encourage their growth.

Similarly, a Swedish group noted:[22]

> An increasing number of people with such a non-industrial occupation complain of the following symptoms: sensation of dry mucous membranes and skin, erythema, mental fatigue, headaches, high frequency of airway infections and cough, hoarseness, wheezing, itching and unspecified hypersensitivity, nausea and dizziness.

These authors ascribed such symptoms to carpeted rooms, and suggested that accumulation of dust and microorganisms should be investigated. Indeed, they found that measured levels of dust and fungi were higher in carpeted rooms, as were reported complaints.

While not directly implicating microorganisms, Finnegan and Pickering include SBS in a review of "building-related

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illness."[19] They discuss a survey they conducted on nine buildings:

> In all the mechanically ventilated buildings, there was a significant excess of work-related headaches, lethargy and nasal and mucous membrane symptoms when compared with the naturally ventilated buildings. In the humidified buildings there was also an excess of work related eye symptoms as well as chest tightness and dry skin, compared to the naturally ventilated buildings.

They also note that the "cause of these work related symptoms in air-conditioned buildings remains to be determined despite much research."

Fungal Illnesses

A Canadian Working Group described three categories of fungal illnesses: respiratory and skin allergies or other damage, tissue infection (pulmonary mycoses), and systemic toxicity (immunosuppression, organ-specific necroses).[23]

One of the fungi most implicated in fungal diseases is Aspergillus, a fungi whose spores are ubiquitous in the environment. The spores may become concentrated in ventilation systems or may be brought into buildings in incoming air. In "normal" individuals exposed to Aspergillus spores, allergic diseases including HP or allergic bronchopulmonary aspergillosis

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may occur.[24] Inhalation of Aspergillus spores may trigger bronchospasm in asthmatics. Superficial and locally invasive infections (ear, skin, sinus, and lung) may also occur. In immune-compromised persons, however, greater invasion from the site of infection may take place.

Many fungi produce mycotoxins, substances which are well-known as carcinogens.[16] Some have reported that mycotoxins may be related to the development of leukemia.[25] In particular, aflatoxin, which may be inhaled in certain circumstances, has been associated with human liver cancer.[26] Similarly, over 500 volatile organic compounds have been identified as being produced by fungi.[26]

Other Infectious Diseases

Some evidence suggests that airborne infectious agents may be spread by ventilation equipment.[27,28] In particular, as Burge notes:[2]

> Indoor infectious aerosols place human occupants at risk because an enclosed space confines and protects the aerosols, which thus can dose the occupant for an extended period.

Elsewhere, Burge writes that influenza, measles and tuberculosis are spread via aerosols, usually in proximity to an infected person; nevertheless, she notes that[20]

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> In poorly ventilated environments, levels can build to the point where susceptible subjects throughout an occupied space become infected. (p. 688, author's emphasis)

A recent study of a Massachusetts building where 27 of 67 occupants (40%) contracted tuberculosis suggested that increasing the outside ventilation rate could have reduced infection rates.[29]

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REFERENCES

1. Committee on Public Health, New York Academy of Medicine,"Resolution Concerning Federal Legislation and Research on Indoor Air Pollution," Bulletin of the New York Academy of Medicine 60: 106-109, 1984.

2. Burge, H.A., "Risks Associated with Indoor Infectious Aerosols," Toxicology and Industrial Health 6: 263-274, 1990.

3. Morey, P.R. and Feeley, J.C., "Microbiological Aerosols Indoors, in Workplaces, Schools, and Homes," ASTM Standardization News Dec. 1988: 54-58, 1988.

4. Morey, P.R., "Experience on the Contribution of Structure to Environmental Pollution." In: Architectural Design and Indoor Microbial Pollution. R.B. Kundsin (ed.). New York, Oxford University Press, 40-80, 1988.

5. Imperato, P.J., "Legionellosis and the Indoor Environment," Bulletin of the New York Academy of Medicine 57: 922-935, 1981.

6. Lee, T.C., Stout, J.E. and Yu, V.L., "Factors Predisposing to Legionella pneumophila Colonization in Residential Water Systems," Archives of Environmental Health 43: 59-62, 1988.

7. "Legionellosis: Position Statement," American Society of Heating, Refrigeration and Air-Conditioning Engineers, Inc. (ASHRAE), February 2, 1989.

8. Muraca, P.W., Stout, J.E., Yu, V.L. and Yee, Y.C., "Legionnaires' Disease in the Work Environment: Implications for Environmental Health," Am Ind Hyg Assoc J 49(11): 584-590, 1988.

9. Barbaree, J.M., "Controlling Legionella in Cooling Towers: Factors Affecting the Transmission of Legionella from Aerosol-Emitting Equipment to People are Described," ASHRAE Journal June 1991: 34-42, 1991.

10. O'Sullivan, P., "Control of Legionnaire's Disease." In: Indoor and Ambient Air Quality. R. Perry and P.W. Kirk (eds.). London, Selper, Ltd., 479-488, 1988.

11. Winn, W.C., "Legionnaires Disease: Historical Perspective," Clinical Microbiology Reviews 1: 60-81, 1988.

2046157496

Source: https://www.industrydocuments.ucsf.edu/docs/qnwl0000

12. O'Mahony, M., Lakhani, A., Stephens, A., Wallace, J.G., Youngs, E.R. and Harper, D., "Legionnaires' Disease and the Sick-Building Syndrome," Epidem Inf 103: 285-292, 1989.

13. Wallace, B., "No Proof Yet of Source of Legionnaire's Disease," The San Francisco Chronicle, A12, September 21, 1991.

"Bacteria Keeps Building Closed," Los Angeles Times, A27, September 21, 1991.

"Second Suspected Outbreak of Legionnaire's Disease Demands Massive Government Intervention, Union Chicago," PR Newswire, September 20, 1991.

Johnson, C., "Legionnaire's Disease Cleanup Moving Slowly, Federal Office May Be Closed Three Weeks," The San Francisco Chronicle, A20, September 20, 1991.

"Legionnaire's Disease Cases Reach Nine," The Associated Press, September 19, 1991.

"Legionnaires' Cases at Building Rise to 9," Los Angeles Times, September 19, 1991.

Johnson, C., "8th New Case of Legionnaire Disease Found," The San Francisco Chronicle, A17, September 19, 1991.

Goodavage, M., "Workers Fear Return to 'Sick Building,'" USA Today, 3A, September 20, 1991.

Anonymous, "Legionnaire's Outbreak Raises Awareness," Indoor Air Quality Update 4(11): 1-3, November 1991.

14. Bardana, E.J., Montanaro, A. and O'Hollaren, M.T., "Building-Related Illness: A Review of Available Scientific Data," Clinical Reviews in Allergy 6: 61-89, 1988.

15. Burge, H.A. and Hodgson, M., "Health Risks of Indoor Pollutants," ASHRAE Journal 30: 34-35, 38, 1982.

16. Solomon, W.R., "Airborne Microbial Allergens: Impact and Risk Assessment," Toxicology and Industrial Health 6: 309-324, 1990.

17. Shellito, J.E., "Hypersensitivity Pneumonitis," Seminars in Respiratory Medicine 12: 196-203, 1991.

18. Lacey, J. and Crook, B., "Fungal and Actinomycete Spores as Pollutants of the Workplace and Occupational Allergens," Annals of Occupational Medicine 32: 515-533, 1988.

2046157497

Source: https://www.industrydocuments.ucsf.edu/docs/qnwl0000

19. Finnegan, M.J. and Pickering, C.A.C., "Review: Building Related Illness," Clinical Allergy 16: 389-405, 1986.

20. Burge, H.A., "Bioaerosols: Prevalence and Health Effects in the Indoor Environment," The Journal of Allergy and Clinical Immunology 86: 687-701, 1990.

21. Rylander, R., Sorensen, S., Goto, H., Yuasa, K. and Tanaka, S., "The Importance of Endotoxin and Glucan for Symptoms in Sick Buildings." In: Present and Future of Indoor Air Quality. C.J. Bieva, Y. Courtois and M. Govaerts (eds.). Amsterdam, Elsevier, 219-226, 1989.

22. Gravesen, S., Larsen, L., Gyntelberg, F. and Skov, P., "Demonstration of Microorganisms and Dust in Schools and Offices: An Observational Study of Non-Industrial Buildings," Allergy 41: 520-525, 1986.

23. Tobin, R.S., Baranowski, E., Gilman, A.P., Kuiper-Goodman, T., Miller, J.D. and Giddings, M., "Significance of Fungi in Indoor Air: Report of a Canadian Working Group." In: Indoor Air '87, Proceedings of the 4th International Conference on Indoor Air Quality and Climate. Berlin, Germany, Volume 1, 718-722, August 17-21, 1987.

24. Bodey, G.P. and Vartivarian, S., "Aspergillosis," European Journal of Clinical Microbiology and Infectious Disease 8: 413-437, 1989.

25. Samson, R.A., "Occurrence of Moulds in Modern Living and Working Environments," European Journal of Epidemiology 1: 54-61, 1985.

26. Miller, J.D., "Fungi as Contaminants in Indoor Air." In: Indoor Air '90: Proceedings of the 5th International Conference on Indoor Air Quality and Climate. Toronto, Canada, Volume 5, 51-64, July 29-August 3, 1990.

27. LaForce, F.M., "Airborne Infections and Modern Building Technology," Environment International 12: 137-146, 1986.

28. Dick, E.C., Jennings, L.C., Mink, K.A., Wartgow, C.D. and Inhorn, S.L., "Aerosol Transmission of Rhinovirus Colds," The Journal of Infectious Diseases 156: 442-448, 1987.

29. Anonymous, "Ventilation and Infectious Diseases--Tuberculosis," Indoor Air Quality Update 4(9): 10, September 1991.

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PHILIP MORRIS RESPONSE TO OSHA RFI

Question 2a(iii): "What data are available that associate adverse health effects with exposure to passive tobacco smoke?"

Summary:

Epidemiologic studies reporting an association between spousal and parental smoking and chronic disease in nonsmokers do not include actual exposure assessments of PTS. Furthermore, available data on exposure suggest that nonsmoker exposures to PTS in public places and workplaces are minimal. Of the 30 epidemiologic studies on spousal smoking and lung cancer, only 12 have assessed reported workplace exposures to PTS; ten of those 12 do not report statistically significant associations between PTS and nonsmoker lung cancer. Only five studies on PTS and heart disease address workplace exposure; not one reports a statistically significant association. Only six studies have investigated workplace PTS exposure and adult respiratory disease; their results can best be described as inconclusive. Similarly, little published data exist on PTS and conditions such as asthma or allergy in the workplace. Furthermore, all the epidemiologic studies on PTS may be criticized for problems in design and methodology and failure to account for possible confounding factors. The available data from published epidemiologic studies are not sufficient to support the claim that PTS exposure in the workplace is associated with chronic disease in nonsmokers.

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PHILIP MORRIS RESPONSE TO OSHA RFI

Question 2a(iii): "What data are available that associate adverse health effects with exposure to passive tobacco smoke?"

Response:

Overview

Epidemiologic studies in the published literature which report an association between spousal or parental smoking and chronic disease (e.g., lung cancer, heart disease, etc.) in nonsmokers are not based upon actual exposure assessments for PTS ("passive" tobacco smoke, also called environmental tobacco smoke (ETS)). Instead, "exposure" is assessed via questionnaire. The notions of "spousal smoking," "parental smoking" or "living with a smoker" are used as surrogate determinants for PTS exposure.

However, data on nonsmoker exposure to PTS are available in the published literature.[1-4,10-13] While these data are independent of the so-called "health effects" (epidemiologic) literature on PTS, they suggest that nonsmoker exposure to PTS in typical public places and workplaces is minimal.[4,10-12,14-15,18-25,33-34,37]

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In addition, the physical and chemical properties of PTS have been essentially ignored and/or misunderstood in a number of published reviews on PTS and disease in nonsmokers. It is important, therefore, to clarify what is available in the scientific literature on the nature of PTS, or, as it is more commonly known, environmental tobacco smoke (ETS).

PTS: A Characterization

Passive tobacco smoke (PTS) is an aged and dilute mixture of sidestream smoke (SS; the smoke from the burning end of the cigarette) and exhaled mainstream smoke (MS; the smoke to which the smoker is exposed). PTS differs chemically and physically from both MS and SS. PTS is a dynamic, ever-changing mixture which, as it ages and dissipates, undergoes chemical reactions and physical change. There is no single definable, reproducibly characterizable entity known as PTS.[1]

Dissipative forces such as air currents and attraction to surfaces influence SS and exhaled MS.[1] Studies indicate that constituents in PTS are hundreds to thousands of times more dilute than either SS or MS. Often, concentrations of PTS constituents fall below detection limits of current scientific measurement devices.

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As PTS ages, a number of physico-chemical changes take place. Matter evaporates from SS particles as they age to PTS. During the aging process, PTS particles coagulate and increase in size. Chemical compounds partition between the gas and particle phase of the smoke. (For example, nicotine is found in the particle phase of MS; in fresh SS, most of the nicotine is in the gas phase.) Decay patterns for constituents of PTS vary over time and are dependent upon physical conditions in the environment.

PTS is not equivalent to either MS or SS. Many studies and reviews employ sidestream/mainstream smoke comparisons, ostensibly to demonstrate the kind and quantity of constituents involved in exposure to PTS. But such comparisons are deceptive and misleading. As two tobacco smoke chemists reported:[1]

> Although ETS originates from sidestream and exhaled mainstream smoke, the great dilution and other changes which these smoke streams undergo as they form ETS make their properties significantly different from those of ETS. Thus, the sidestream/mainstream ratios quoted in Table 1 can be misleading if used out of context. The important question is not the ratio of sidestream/mainstream but rather what is the concentration of the constituent in the indoor environment and how does it compare to levels from sources other than ETS. Studies based solely on observations of fresh sidestream, or highly and unrealistically concentrated ETS, should take into account the possible differences between these smokes and ETS found in real-life situations.

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Even the 1986 Report of the Surgeon General on PTS conceded:

> Comparison of the relative concentrations of various components of SS and MS smoke provides limited insights concerning the toxicological potential of ETS in comparison with active smoking. As described above, SS characteristics, as measured in a chamber, do not represent those of ETS, as inhaled by the non-smoker under non-experimental conditions.[2]

Similarly, the 1986 NAS/NRC Report on ETS concluded:

> Because the physicochemical nature of ETS, MS, and SS differ, the extrapolation of health effects from studies of MS or of active smokers to nonsmokers exposed to ETS may not be appropriate.[3]

Exposure to PTS

Published studies indicate that nonsmoker exposure to PTS under normal, everyday conditions is minimal. For example, researchers report that there is little difference in ambient levels of carbon monoxide in smoking and nonsmoking areas of workplaces and public places and in homes with and without smokers.[4-9] Other studies indicate that PTS contributes approximately 30% of the total

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particles in the air of a typical public place.*[4,10,11,12,14,15] Nicotine is often used as a marker for PTS exposures because it is unique to tobacco smoke. Typical measurements of nicotine range from an exposure equivalent of 1/100 to less than 1/1,000 of one filter cigarette per hour.[18-25] This means that a nonsmoker would have to spend from 100 to 1,000 hours or more in an office, restaurant or public place in order to be exposed to the nicotine equivalent of a single cigarette.

Studies which have examined PTS constituent levels of nitrosamines, nitrogen oxides and volatile organic compounds (such

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* A paper published in a 1980 issue of Science magazine, in which the authors reported the results of their efforts to measure particles or particulates in the air of smoking and nonsmoking areas, is often cited to support the claim that ETS is a major indoor pollutant. The authors, Repace and Lowrey, contend that the levels of particles they observed in the smoking areas were much higher than in the nonsmoking areas. However, their study results are inconsistent with many others. For example, the average particle count attributed to ETS in their study was from three to twenty times higher than the average levels reported in other studies of office buildings, restaurants and residences.

There are a number of explanations for the authors' apparent overestimation of ETS exposure. First, they selectively sampled environments such as meeting and game rooms, bars, and sandwich shops which did not represent normal occupancy conditions and where particulate levels would likely be high regardless of the presence or absence of tobacco smoke. Second, through inappropriate testing methods, they incorrectly assumed all particles in the air arose from ETS. However, as several researchers have noted, ETS typically contributes about one-third of the overall particle levels in indoor spaces. Moreover, particles also are generated by people and their everyday routine activities such as movement and cooking. (Repace, J. and A. Lowrey, "Indoor Air Pollution, Tobacco Smoke and Public Health," Science 208: 464-472, 1980.)

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as benzene**) report minimal contributions to overall ambient air levels in homes, the workplace and public places.[26-39]

Questionnaire Reliability

All of the epidemiologic studies on the purported associations between living with a smoker and disease in nonsmokers rely solely upon questionnaire responses about reported exposure, rather than upon actual PTS exposure data. Recent studies indicate that questionnaires are an extremely unreliable and inaccurate measure of exposure.[40-42] Questionnaire responses about exposure vary widely when compared with actual measurements of PTS constituents in the ambient air.[42]

** Benzene exposure from ETS is negligible, despite reports to the contrary. "Automotive fuel is, by far, the largest, most pervasive source of benzene exposure. In 1989, the U.S. Department of Health and Human Services estimated that 1 billion pounds of benzene were released into the atmosphere from the refueling and operation of approximately 130 million motor vehicles in 1976 [NIEHS, 1989]. This translates into 7.8 pounds of benzene per vehicle per year. In contrast, a pack-per-day smoker would generate approximately 0.008 pounds of benzene per year, assuming that, at most, 0.5 mg of benzene is generated from one cigarette (MS plus SS) [Hoffmann, 1990]. Based on these estimates, an average person is potentially exposed to 1,000 times more ambient benzene from one automobile than from a smoker in a given year." [From: Response of R.J. Reynolds to the U.S. EPA: "ETS: A Guide to Workplace Smoking Policies," October 1, 1990.]

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In a review paper referenced in the OSHA RFI (RFI, Reference #7), Tager assessed the reliability of questionnaire responses as a surrogate for actual exposure data.[43] He writes:

> Questionnaires theoretically suffer from potential problems of recall bias, inaccurate recall, and false reporting of personal tobacco use.

And:

> Among the most significant limitations of existing questionnaire data are the facts that many of the questions were not designed specifically to investigate involuntary exposure, or the questionnaires have been incomplete in their probing of the circumstances of exposure. These limitations have made it difficult to provide even semi-quantitative exposure estimates over time.

In a series of studies,[40-42] Coultas et al., compared actual PTS exposure data with questionnaire response estimates of exposure. They report:

> Responses concerning recent tobacco smoke exposure and urinary cotinine levels were correlated to only a modest degree. The authors conclude that adults can reliably report whether household members smoked during their childhood, but information on quantitative aspects of smoking is reported less reliably.

And:

> Not surprisingly, we found that the questionnaire responses were poor predictors

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> of concentrations of respirable particles and nicotine.
>
> During one workshift, we obtained questionnaires on exposure, saliva and urine for cotinine, and personal air samples for respirable particles and nicotine. The levels of cotinine, respirable particles, and nicotine varied widely with self-reports of exposure to ETS . . . .

In 1983, Friedman et al. examined the accuracy of self-reported exposure to PTS.[44] They observed:

> Although the reported passive smoking of married persons was strongly related to their spouses' habits, categorization by spouses' smoking resulted in considerable misclassification.

Specifically, they reported:

> Our data also indicate that studies of the effects of passive smoking should consider the correlates of this form of smoke exposure before concluding that it is responsible for some observed effect.
>
> However, using the spouse's smoking status to classify persons resulted, as far as can be discerned with our relatively crude questionnaire, in a considerable amount of misclassification. About 40-50 per cent of persons with nonsmoking spouses reported some passive exposure and, conversely, 30-35 per cent who were married to smokers surprisingly reported no exposure.

Pron et al.,[45] in a study on the reliability of self-reported PTS exposure histories, observed the following:

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> Responses to initial screening questions used to detect a person's exposure to passive smoke were more reliable for residential than for occupational exposure.

And:

> Quantitative measures of exposure to passive smoke, i.e., number and duration of exposure, were even less reliably reported.
>
> Test-retest estimates of reliability suggests that misclassification of such exposures may be extensive.

They concluded:

> The results of this study suggest that improvements in the reliability of measurement of exposures to passive smoke are needed for future studies.

Most recently, the National Academy of Sciences, in their 1991 Report, "Human Exposure Assessment for Airborne Pollutants: Advances and Opportunities," addressed the validity of questionnaires for exposure assessment in studies of PTS. The Report states:[46]

> It is important to examine ways to improve techniques to assess more accurately exposure to ETS.
>
> Until recently, epidemiological studies of the acute and chronic health effects of ETS have been handicapped by limitations in assessing exposures to ETS. Exposures occur at a wide

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range of concentrations for highly variable periods and in numerous indoor environments. Unlike active smoking, exposure to ETS cannot now be easily assessed with standardized methods. Previous epidemiological studies of the chronic effects of ETS, particularly lung cancer, have determined exposure solely by questionnaires, which have not been standardized or validated. The questionnaires have usually obtained information on smoking habits of occupants of residences to permit assessment of ETS exposures and have not adequately addressed the impact of occupational exposures. The use of such questionnaires might pose problems in misclassification of subjects by exposure status and obscure possible exposure-effect relationships.

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Source: https://www.industrydocuments.ucsf.edu/docs/qnwl0000

REFERENCES

1. Baker, R. and Proctor, C., "The Origins and Properties of Environmental Tobacco Smoke," Env Int (16): 231-245, 1990.

See also:

Löfroth, G., et al., "Characterization of Environmental Tobacco Smoke," Env Sci Technol (23): 610-614, 1989.

Reasor, M. and Will, J., "Assessing Exposure to Environmental Tobacco Smoke: Is It Valid to Extrapolate from Active Smoke?," Journal of Smoking Related Diseases 2(1): 111-127, 1991.

Proctor, C. and Dymond, H., "The Measurement of ETS Through Adsorption/Desorption Procedures." In: Indoor Air Quality. H. Kasuga (ed.). Springer-Verlag, Berlin, Heidelberg, 82-89, 1990.

Nystrom, C., et al., "Assessing the Impact of Environmental Tobacco Smoke on Indoor Air Quality: Current Status." In: Proceedings of the ASHRAE Conference, IAQ '86. April 20-23, 1986, Atlanta, Georgia, 213-233, 1986.

Rawbone, R., "The Aging of Sidestream Tobacco Smoke Components in Ambient Environments." In: Indoor Air Quality. H. Kasuga (ed.). Springer-Verlag, Berlin, Heidelberg, 55-61, 1990.

Piade, J., et al., "Assessment of ETS Impact on Office Air Quality." In: Indoor Air Quality. H. Kasuga (ed.). Springer-Verlag, Berlin, Heidelberg, 112-119, 1990.

Scherer, G., et al., "Importance of Exposure to Gaseous and Particulate Phase Components of Tobacco Smoke in Active and Passive Smokers," Occup Env Health (62): 459-466, 1990.

2. U.S. Department of Health and Human Services, A Report of the Surgeon General, The Health Consequences of Involuntary Smoking, 24, 1986.

3. Committee on Passive Smoking, Board on Environmental Studies and Toxicology, National Research Council, Environmental Tobacco Smoke, Measuring Exposures and Assessing Health Effects. National Academy Press, Washington, D.C., 7-8, 1986.

4. Kirk, P., et al., "Environmental Tobacco Smoke in Indoor Air." In: Indoor and Ambient Air Quality. R. Perry and P. Kirk (eds.). London, Selper Ltd., 99-112, 1988.

2046157511

Source: https://www.industrydocuments.ucsf.edu/docs/qnwl0000

5. Duncan, D. and Greavey, P., "Passive Smoking and Uptake of Carbon Monoxide in Flight Attendants," JAMA 251(20): 120-21, 1984.

6. Cox, B. and Whichelow, M., "Carbon Monoxide Levels in the Breath of Smokers and Nonsmokers: Effect of Domestic Heating Systems," J Epidemiol Community Health 39: 75-78, 1985.

7. Girman, J. and Traynor, G., "Indoor Concentrations," JAPCA 33(2): 89, 1983.

8. Yocom, J., "Indoor Concentrations," JAPCA 33(2): 89, 1983.

9. Nitta, H., et al., "Measurements of Indoor Carbon Monoxide Levels Using Passive Samplers in Korea." In: Indoor Air '90. The Fifth International Conference on Indoor Air Quality and Climate, Toronto, Canada, July 29-August 3, 77-82, 1990.

10. Carson, J. and Erikson, C., "Results from Survey of Environmental Tobacco Smoke in Offices in Ottawa, Ontario," Environ Technol Letters 9: 501-508, 1988.

11. Sterling, T., et al., "Environmental Tobacco Smoke and Indoor Air Quality in Modern Office Work Environments," Journal of Occupational Medicine 26(1): 57-62, 1987.

12. Sterling T. and Mueller, B., "Concentrations of Nicotine, RSP, CO and CO_2 in Nonsmoking Areas of Offices Ventilated by Air Recirculated From Smoking Designated Areas," Am Ind Hyg Assoc J 49(9): 423-426, 1988.

13. Hosein, R., "The Relationship Between Pollutant Levels in Homes and Potential Sources." In: Indoor Air Quality in Cold Climates, Hazards and Abatement Measures. D. Walkinshaw (ed.). APCA, Ottawa, Ontario, 250-260, 1985.

14. Proctor, C., et al., "Measurements of Environmental Tobacco Smoke in an Air-Conditioned Office Building," Environ Technol Letters (10): 1003-1018, 1989.

15. Oldaker, G., et al., "Results From Surveys of Environmental Tobacco Smoke in Restaurants." In: Indoor Air Quality. H. Kasuga (ed.). Springer-Verlag, Berlin, Heidelberg, 99-104, 1990.

16. Spengler, J., "Harvard's Indoor Air Pollution Health Study." In: Indoor Air Quality. H. Kasuga (ed.). Springer-Verlag, Berlin, Heidelberg, 241-248, 1990.

2046157512

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17. Quackenboss, J. and Lebowitz, M., "Indoor-Outdoor Relationships for Particulate Matter: Exposure Classifications and Health Effects," Environ Int 15: 353-360, 1989.

18. Hinds, W. and First, M., "Concentrations of Nicotine and Tobacco Smoke in Public Places," New England Journal of Medicine 292(16): 844-845, 1975.

19. Badre, R., et al., "Pollution Atmospherique par la Fumee de Tabac (Atmospheric Pollution by Smoking)," Ann Pharm Fr 36(9-10): 443-452, 1978. Translation.

20. Jenkins, R., et al., "Development and Application of a Thermal Desorption-Based Method for the Determination of Nicotine in Indoor Environments." In: Indoor and Ambient Air Quality. R. Perry and P. Kirk (eds.). London, Selper Ltd., 557-566, 1988.

21. Muramatsu, M., et al., "Estimation of Personal Exposure to Tobacco Smoke with a Newly Developed Nicotine Personal Monitor," Environ Res 35: 218-227, 1984.

22. Muramatsu, M., et al., "Estimation of Personal Exposure to Ambient Nicotine in Daily Environment," Arch Occup Environ Health 59: 545-550, 1987.

23. Thompson, C., et al., "A Thermal Desorption Method for the Determination of Nicotine in Indoor Environments," Envir Sci Tech 23: 429-435, 1989.

24. Foliart, D., et al., "Passive Absorption of Nicotine in Airline Flight Attendants," New England Journal of Medicine 308(18): 1105, 1983.

25. Oldaker, G. and Conrad, F., "Estimation of the Effect of Environmental Tobacco Smoke on Air Quality Within Passenger Cabins of Commercial Aircraft," Envir Sci Tech 21: 994-999, 1987.

26. Lehnert, G., "Conclusion: In the Realm of Speculation," Munch med Wschr 124(4), 1982.

27. Schievelbein, H., "Are There Really Important New Findings About Passive Smoking?," Oeff Gesundheitswes 44(0): 454-56, 1982. Translation.

28. Stehlik, G., et al., "Concentration of Dimethylnitrosamine in the Air of Smoke-Filled Rooms," Ecotoxicol Environ Safety 6: 495-500, 1982.

2046157513

Source: https://www.industrydocuments.ucsf.edu/docs/qnwl0000

29. Sega, K. and Fugas, M., "Nitrogen Dioxide Concentrations in Residences." In: Indoor and Ambient Air Quality. R. Perry and P. Kirk (eds.). London, Selper Ltd., 493-496, 1988.

30. Good, B., et al., "Effect of Cigarette Smoking on Residential NO_2 Levels," Environ Int 8: 167-175, 1982.

31. Shimizu, Y., et al., "Influence of Indoor Air Pollution on NO_2 Personal Exposure Levels of Schoolchildren." In: Present and Future of Indoor Air Quality. C. Bieva, et al. (eds.). Brussels, Elsevier, 337-345, 1989.

32. Hendel-Kramer, A., et al., "Regression Model for Indoor Concentrations of Combustion-Generated Gases." In: Present and Future of Indoor Air Quality. C. Bieva, et al. (eds.). Brussels, Elsevier, 315-320, 1989.

33. Bayer, C. and Black, M., "Thermal Desorption/Gas Chromatographic/Mass Spectrometric Analysis of Volatile Organic Compounds in the Offices of Smokers and Nonsmokers," Biomed and Envir Mass Spect 14(8): 363-367, 1987.

34. Proctor, C., et al., "Measurements of Environmental Tobacco Smoke in an Air-Conditioned Office Building," Environ Technol Letters (10): 1003-1018, 1989.

35. Godish, T., "Formaldehyde Exposures from Tobacco Smoke: A Review," AJPH 79(8): 1044-1045, 1989.

36. Godish, T., "Residential Formaldehyde: Increased Exposure Levels Aggravate Adverse Health Effects," Journal of Environmental Health 53(3): 34-35, 1990.

37. Adlkofer, F., et al., "Significance of Exposure to Benzene and Other Toxic Compounds Through Environmental Tobacco Smoke," J Cancer Res Clin Oncol (116): 591-598, 1990.

38. Hugod, C., et al., "Exposure of Passive Smokers to Tobacco Smoke Constituents," Int Arch Occup Environ Health (42): 21-29, 1978.

39. Proctor, C., et al., "Measurement of Environmental Tobacco Smoke in an Air-Conditioned Office Building." In: Present and Future of Indoor Air Quality. C.J. Bieva, et al. (eds.). Brussels, Elsevier, 169-172, 1989.

40. Coultas, D., et al., "Questionnaire Assessment of Lifetime and Recent Exposure to Environmental Tobacco Smoke," American Journal of Epidemiology 130(2): 338-347, 1989.

2046157514

Source: https://www.industrydocuments.ucsf.edu/docs/qnwl0000

41. Coultas, D., et al., "Variability of Measures of Exposure to Environmental Tobacco Smoke in the Home," American Review of Respiratory Disease 142: 602-606, 1990.

42. Coultas, D., et al., "A Personal Monitoring Study to Assess Workplace Exposure to Environmental Tobacco Smoke," American Journal of Public Health 80(8): 988-990, 1990.

43. Tager, I., "Health Effects of Involuntary Smoking in the Workplace," New York State Journal of Medicine 89(1): 27-31, 1989.

44. Friedman, G. et al., "Prevalence and Correlates of Passive Smoking," American Journal of Public Health 73(4): 401-405, 1983.

45. Pron, G. et al., "The Reliability of Passive Smoking Histories Reported in a Case-Control Study of Lung Cancer," American Journal of Epidemiology 127(2): 267-273, 1988.

46. National Academy of Sciences, National Research Council, Committee on Advances in Assessing Human Exposure to Airborne Pollutants, Human Exposure Assessment for Airborne Pollutants: Advances and Opportunities, National Academy Press, Washington D.C., 215-216, 1991.

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Response to Question 2a(iii) (continued):

Lung Cancer

It has been argued that "passive" tobacco smoke (PTS) exposure increases the risk of lung cancer in nonsmokers.[1,2] This claim is based upon data from epidemiologic studies of women who report spousal smoking in the home. The studies cited in support of the claimed association between spousal smoking and lung cancer have been heavily criticized in the scientific literature. For example, of the 30 published epidemiologic studies examining the issue of spousal smoking and lung cancer in nonsmokers, none actually measured exposure to PTS. Also, the risk estimates reported in the studies are "weak" in epidemiologic terms (i.e., less than 3.0). Twenty-four of the 30 studies do not achieve statistical significance; that is, their conclusions are consistent with a null hypothesis of no association. In fact, nine of the spousal smoking studies report risk estimates that are negative (i.e., less than 1.0); one of these is statistically significantly negative. Moreover, studies on spousal smoking are of questionable relevance to the workplace.

To date, 12 of the 30 published epidemiologic studies on the issue of spousal smoking and lung cancer in nonsmokers have assessed reported workplace exposures to "passive" tobacco smoke (PTS). Ten of the 12 studies report associations between PTS and

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nonsmoker lung cancer which do not achieve statistical significance; only two studies report marginally statistically significant increased risks for persons who reported exposure to PTS in the workplace. **Thus, the existing data examining reported workplace PTS exposures and lung cancer incidence in nonsmokers are consistent with the null hypothesis of no association.**

Description of Studies

Of the 12 epidemiologic studies on spousal smoking which assess an estimate of workplace PTS exposure, six were performed in the United States, three in European countries and three in Asian countries. The following are brief descriptions of these studies and their conclusions regarding workplace PTS exposure. The studies, their reported point (risk) estimates for workplace PTS exposure, and the statistical significance of their point estimates are summarized in Table 1 (immediately following page 14).

In 1984, Kabat and Wynder published results of a case-control study of hospitalized individuals, mostly from New York City.[3] A total of 25 male cases and 53 female cases and their matched controls were included. The authors wrote:

> The plausibility of a role of passive inhalation in lung cancer can be questioned on several grounds . . .

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> Cases do not differ from controls except for the greater exposure to cigarette smoke at work reported by male cases compared to male controls.

The authors reported that 18 of 25 male cases versus 11 of 25 controls reported being exposed to PTS in the workplace. This result was marginally statistically significant at P = 0.05. The authors' reported results for women are inconsistent with their conclusions on men; 26 of 53 female cases versus 31 of 53 controls (i.e., fewer cases than controls) reported exposure in the workplace. This result is not statistically significant.

The second U.S. study, by Garfinkel and colleagues, was a case-control study of hospitalized women in New Jersey and Ohio.[4] It included the following estimation of workplace exposure to PTS:

> The interviewer also asked about the average number of hours a day the woman had been exposed to the smoke of others at any time during the past five years, during the past 25 years at home, while at work . . .

The authors reported the following:

> [The] OR for exposure at work during the last five years was 0.88 [95% CI 0.66, 1.18; 14 cases, 52 controls]; for the last 25 years, it was 0.93 [95% CI 0.73, 1.18; 34 cases, 118 controls].

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These two point estimates represent negative associations between reported PTS exposures in the workplace and lung cancer in nonsmokers.

In 1985, Wu and colleagues reported on a case-control study of women in a Los Angeles, CA tumor registry.[5] For adenocarcinoma, the authors report, "we did not observe any elevated risk associated with passive smoke exposure . . . at work (RR = 1.3; 95% CI = 0.5-3.3)."

Conclusions based on a case-control study of 191 men and women in New York State were reported in 1990 by Janerich and colleagues,[6] who wrote:

> Exposure in the workplace was measured by recording the number of smokers who worked with each study subject during his or her lifetime and the amount of time the subjects spent working with these smokers. These exposures were compared for case patients and control subjects. Estimating the odds ratio as a continuous variable for an equivalent differential of 150 person-years of exposure gave an odds ratio of 0.91 (95 percent confidence interval, 0.80 to 1.04), indicating no evidence of adverse effect of environmental tobacco smoke in the workplace.

In 1990, Kabat reported preliminary results from an American Health Foundation case-control study, which then included 90 cases and 247 controls.[7] Kabat reported that "preliminary

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analyses of the data do not indicate any striking ETS exposure differences between cases and controls." Specifically, he reported odds ratios for men of 0.98 (95% CI 0.46, 2.10) and for women of 1.00 (0.49, 2.06).

The most recent American study was published in 1991 by Fontham and colleagues.[8] It represents a preliminary report on a case-control study of women in five U.S. cities. For all lung cancer types combined, an odds ratio of 1.34 (95% CI 1.03, 1.73) was reported for those women who reported that they were ever exposed to PTS in an occupational setting.

The first European study including an assessment of PTS exposure in the workplace and nonsmoker lung cancer was published in 1984.[9] The authors wrote that "overall the results showed no evidence of an effect of passive smoking on lung cancer incidence among lifelong nonsmokers," although they presented no odds ratios for workplace exposure.

In 1989, Svensson and colleagues reported on their case-control study of women in Stockholm County, Sweden.[10] For women exposed at home or at work (17 cases and 90 controls), the authors reported a statistically nonsignificant odds ratio of 1.2 (95% CI 0.4, 2.9). For women exposed at home and at work (7 cases and 24 controls), the reported odds ratio was 2.0 (95% CI 0.6, 8.1).

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The third European case-control study to assess workplace exposure was conducted on hospitalized women in Athens, Greece.[11] Based on 89 cases and 118 controls, the authors conclude: "The effect of exposure to passive smoking at work was very small and not statistically significant (the RR between extreme quartiles was 1.08 (0.24-4.87))."

Koo and colleagues, in their 1987 case-control study of women in Hong Kong, included an assessment of workplace exposure in an accounting of total lifetime exposure to PTS.[12] The authors concluded:

> On the basis of our extensive life-history data, we were able to calculate the total years, hours, mean hours/day, and cigarettes/day to which the subjects had been exposed to tobacco smoke at home or at work.
>
> Despite such detailed accounting, we were unable to find a significant trend in the crude or adjusted RR for these 4 lifetime measurements of passive smoking.

Shimizu, et al.,[13] reported that in their case-control study of 90 women in Nagoya, Japan:

> Passive smoke exposure at work was not clearly associated with female lung cancer, although the relative risk was slightly elevated (RR = 1.2).

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That reported relative risk was not statistically significant.

A joint Chinese-American study of women in Shenyang and Harbin, two industrial cities in northeast China, reported that 228 cases and 301 controls had been exposed to PTS in the workplace.[14] A relative risk of 1.1 (95% CI 0.9, 1.6) was calculated, which the authors described as a "small excess risk," although it was not statistically significant. The authors also noted that "there were no significant dose-response trends associated with years of passive smoke exposure at work."

Bias and Confounding Factors in Studies on Spousal Smoking

The epidemiologic studies on spousal smoking and lung cancer[3-32] have been criticized for their failure to account for a variety of biases and confounding factors that could affect the validity of their reported findings. In their discussion of such studies, for example, American researchers Ernst Wynder and Geoffrey Kabat cautioned that "if the observed relative risk is small," which they note is "the case" in the reported associations between spousal smoking and lung cancer, "it is important to determine whether the effect could be due to biased selection of subjects, confounding, biased reporting, or anomalies of particular subgroups."[33]

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Misclassification of exposure may contribute to the reported increase in lung cancer risks among nonsmokers, according to several scientists. For example, none of the studies on PTS and lung cancer provides direct observational information on PTS exposures. Instead, spouses, next-of-kin or friends were asked to estimate the amount of PTS to which they thought the subject was exposed. Such estimates may result in what is called exposure misclassification, which several researchers have reported leads to improper indices of exposure and incorrect estimations of risk.[4,34-39] In Garfinkel's study, for example, the reported risk for lung cancer in the women exposed to PTS was actually less than for women not exposed when either the women's or their husbands' estimates were used.[4] Other authors, including the National Research Council, have recently criticized questionnaires used in PTS studies for not being standardized or validated; they pointed out that misclassification of exposure may occur if the questionnaire is not appropriately designed.[40-42]

Biostatistician S. James Kilpatrick has identified another form of misclassification, called differential misclassification, which results "from the tendency of respondents to inflate the amount of ETS exposure for lung cancer cases and deflate the report of exposure for controls."[34] Similarly, Dr. Ernst Wynder, President of the American Health Foundation, notes that "relatives of a

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nonsmoking lung cancer patient are more likely to report passive inhalation exposure on the part of their relative than are relatives of a control patient."[43] Wynder and a co-author also noted that even if the patient herself is interviewed, some overreporting of PTS exposure may occur.[44]

Misclassification of case studies can also arise if diagnoses of lung cancer are not histologically confirmed.[45] Without histologic confirmation, a tumor arising at another site and metastasizing or traveling to the lung could be erroneously identified as a primary lung tumor.

A more subtle form of potential bias, known as "publication bias," stems from the apparent unwillingness of scientific and medical journals to publish studies which report negative or weakly positive results.[46-48] Scientists have recently expressed concern over the growing trend among such journals to overemphasize (and hence to publish) only those studies which report positive increases in risk.[49,50] Published studies which are combined for meta-analyses, therefore, may not truly represent all investigations on the issue of PTS exposure and lung cancer.[51]

Statistician and epidemiologist Peter Lee has argued that the increased risks reported in the various studies are the result of an inherent bias in study design rather than the result

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of any genuine effect from exposure to PTS.[52-59] In his analyses, Lee has presented data which indicate that the reported risks cannot be explained on the basis of either PTS exposure or dose for the nonsmoker. Rather, he contends that the reported "risks" are the result of bias caused by a small number of smokers who are misclassified in the studies as nonsmokers.

Moreover, most of the epidemiological studies on ETS and lung cancer have failed to consider age differences, diet, occupation and exposures to indoor or outdoor pollution as potential confounding elements. The importance of such factors is increasingly underscored in more recent publications.[60,61]

In developing countries, for example, the use of kerosene, gas, coal, liquefied petroleum gas, straw or wood for heating and cooking reportedly contributes to elevated levels of certain indoor air constituents, and may lead to increases in disease incidence.[62,63] Early, limited reports first suggested that exposures to indoor air constituents may be responsible for the increased risk of lung cancer among Oriental women.[64,65] Since then, a number of studies have reported elevated risks for lung cancer associated with the use of coal in stoves and other indigenous heating devices in China.[14,29,32,66-72] At least two papers have reported that certain cooking techniques which produce oil vapors, e.g., stir-frying and deep frying, were associated

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with increased lung cancer risks among Chinese women.[14,25] Another paper reported that national air quality standards were consistently exceeded in the Chinese kitchens studied.[73] Similarly, the use of kerosene, coal, wood or straw has been associated with an increased risk of lung cancer in Japanese women.[27,30] It appears that poor indoor air quality may not be restricted to Asian countries; similar observations regarding workplaces and offices have been made in Greece as well.[74]

In addition to poor indoor air quality from heating and cooking fuels, at least one epidemiologic study from northeast China reported statistically significant associations between outdoor air pollution and lung cancer incidence.[72]

Several aspects of diet have been suggested to be possible confounding factors. For instance, Dr. Linda Koo, in several papers published between 1988 and 1990, re-analyzed her data on nonsmoking wives of smokers.[75-78] Her results indicated that wives of nonsmoking husbands had "healthier" lifestyles than wives of smoking husbands; they exhibited higher socio-economic status and had better indices of family cohesiveness and lower frequencies of selected health problems and complaints. An important and statistically significant difference was reportedly found in the diets of the two groups. Wives of smoking husbands consumed more processed and spicy foods and ate fewer fresh fruits and vegetables

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than wives of nonsmoking men. Koo concluded that such correlates of smoking status "act as important confounders when evaluating health risks among families with smoking husbands." She also wrote:

> [C]aution should be exercised when interpreting data on ETS. It may not be the hazards of tobacco smoke that are being evaluated, but a whole range of behaviors that result from having a smoking husband, which may in turn increase the risk for certain diseases among their wives and children.[75]

Moreover, in 1989, Sidney and colleagues reported that nonsmokers living with smokers consumed less carotene (Vitamin A) than nonsmokers who lived with other nonsmokers. They concluded that "dietary beta-carotene intake is a potential confounder and should be measured whenever possible in studies of the relation between passive smoking and lung cancer."[79] In 1991, additional supportive data were provided by Le Marchand and colleagues' study of women in Hawaii, which found that beta-carotene intake was inversely associated with PTS exposure.[80] The authors noted: "Decreased beta-carotene consumption could explain, in part or in total, the moderately elevated lung-cancer risk observed for passive smokers in past studies." In addition, in a 1990 abstract, Waller and Smith reported a correlation between serum beta-carotene level and socioeconomic status, suggesting that the relationship may be even more complex.[81] Another aspect of diet, namely, consumption of green tea, was associated with a statistically significant

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increased risk of lung cancer in women in Hong Kong.[82] Similar results were first reported at a 1987 conference in Tokyo, in a paper calling for increased attention to possible relationships between substances taken in orally and lung cancer.[83]

Other potential confounders in studies of PTS and lung cancer include occupational exposures;[13,14,29,80,84] personal health factors (e.g., menstrual cycle length, history of respiratory disease);[14,29,32,78] family history of lung cancer;[29,55] and even keeping pet birds.[85] More than 20 independent risk factors for lung cancer were listed in a recent article by Gori and Mantel.[86] These authors pointed out that:

> Since many of the RRs [for those risk factors] are substantially larger than any reported for the association of lung cancer and ETS, even weak contributions by combinations of these confounders would be cumulative and could be more than sufficient to explain the marginal lung cancer risks that some epidemiologic studies of ETS have reported. In fact it is likely to be so, because these studies have not controlled for the factors in any meaningful or comprehensive way, while other investigations provide evidence that several of those risk factors cluster and selectively segregate in families with smokers.

Swedish scientist Ragnar Rylander summed up the importance of confounders in a 1990 article.[61] He cautioned that studies evaluating the relationship between exposure to ETS and lung cancer "must take into account other environmental risk or protection

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factors and the possibility that exposure to environmental tobacco smoke may be confounded," which he noted "has not been considered in the majority of such studies." He concluded: "Until this has been done, the claim of causality between environmental tobacco smoke and lung cancer remains uncertain."

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REFERENCES

1. U.S. Department of Health and Human Services, Public Health Service, Office on Smoking and Health, The Health Consequences of Involuntary Smoking: A Report of the Surgeon General. DHHS Publication No. (CDC) 87-8398, Washington, D.C., U.S. Government Printing Office, 1986.

2. U.S. Environmental Protection Agency, Office of Health and Environmental Assessment, Office of Atmospheric and Indoor Air Programs, Health Effects of Passive Smoking: Assessment of Lung Cancer in Adults and Respiratory Disorders in Children, External Review Draft, EPA 600/6-90/006A, May, 1990.

3. Kabat, G. and Wynder, E., "Lung Cancer in Nonsmokers," Cancer 53(5): 1214-1221, 1984.

4. Garfinkel, L., Auerbach, O. and Joubert, L., "Involuntary Smoking and Lung Cancer: A Case-Control Study," Journal of the National Cancer Institute 75(3): 463-469, 1985.

5. Wu, A., Henderson, B.E., Pike, M.C. and Yu, M.C., "Smoking and Other Risk Factors for Lung Cancer in Women," Journal of the National Cancer Institute 74(4): 747-751, 1985.

6. Janerich, D., Thompson, W.D., Varela, L.R., Greenwald, P., Chorost, S., Tucci, C., Zaman, M.B., Melamed, M.R., Kiely, M. and McKneally, M.F., "Lung Cancer and Exposure to Tobacco Smoke in the Household," New England Journal of Medicine 323: 632-636, 1990.

7. Kabat, G.C., "Epidemiologic Studies of the Relationship Between Passive Smoking and Lung Cancer." In: Toxicology Forum: 1990 Annual Winter Meeting. Washington, D.C., 187-199, February 19-21, 1990.

8. Fontham, E.T.H., Correa, P., Wu-Williams, A., Reynolds, P., Greenberg, R.S., Buffler, P.A., Chen, V.W., Boyd, P., Alterman, T., Austin, D.F., Liff, J. and Greenberg, S.D., "Lunc Cancer in Nonsmoking Women: A Multicenter Case-Control Study," Cancer Epidemiology, Biomarkers & Prevention 1: 35-43, 1991.

9. Lee, P.N., Chamberlain, J. and Alderson, M.R., "Relationship of Passive Smoking to Risk of Lung Cancer and Other Smoking-Associated Diseases," British Journal of Cancer 54: 97-105, 1986.

2046157531

Source: https://www.industrydocuments.ucsf.edu/docs/qnwl0000

10. Svensson, C., Pershagen, G. and Klominek, J., "Smoking and Passive Smoking in Relation to Lung Cancer in Women," Acta Oncologica 28(5): 623-639, 1989.

11. Kalandidi, A., Katsouyanni, K., Voropoulou, N., Bastas, G., Saracci, R. and Trichopoulos, D., "Passive Smoking and Diet in the Etiology of Lung Cancer Among Non-Smokers," Cancer Causes and Control 1: 15-21, 1990.

12. Koo, L.C., Ho, J.H.-C., Saw, D. and Ho, C.Y., "Measurements of Passive Smoking and Estimates of Lung Cancer Risk Among Non-Smoking Chinese Females," International Journal of Cancer 39: 162-169, 1987.

13. Shimizu, H., Morishita, M., Mizuno, K., Masuda, T., Ogura, Y., Santo, M., Nishimura, M., Kunishima, K., Karasawa, K., Nishiwaki, K., Yamamoto, M., Hisamichi, S. and Tominaga, S., "A Case-Control Study of Lung Cancer in Nonsmoking Women," Tohoku Journal of Experimental Medicine 154: 389-97, 1988.

14. Wu-Williams, A.H., Dai, X.D., Blot, W., Xu, Z.Y., Sun, X.W., Xiao, H.P., Stone, B.J., Yu, S.F., Feng, Y.P., Ershow, A.G., Sun, J., Fraumeni, J.F and Henderson, B.E., "Lung Cancer Among Women in North-East China," British Journal of Cancer 62: 982-987, 1990.

15. Hirayama, T., "Non-Smoking Wives of Heavy Smokers Have a Higher Risk of Lung Cancer: A Study from Japan," British Medical Journal 282: 183-185, 1981.

16. Trichopoulos, D., Kalandidi, A., Sparros, L. and MacMahon, B., "Lung Cancer and Passive Smoking," International Journal of Cancer 27(1): 1-4, 1981.

17. Garfinkel, L., "Time Trends in Lung Cancer Mortality Among Nonsmokers and a Note on Passive Smoking," Journal of the National Cancer Institute 66(6): 1061-1066, 1981.

18. Chan, W.C. and Fung, S.C., "Lung Cancer in Non-Smokers in Hong Kong." In: Cancer Campaign Vol. 6, Cancer Epidemiology. E. Grundmann (ed.). Stuttgart, Gustav Fischer Verlag, 199-202, 1982.

19. Correa, P., Pickle, L.W., Fontham, E., Lin, Y. and Haenszel, W., "Passive Smoking and Lung Cancer," Lancet II: 595-597, 1983.

20. Buffler, P.A., Pickle, L.W., Mason, T.J. and Contant, C., "The Causes of Lung Cancer in Texas." In: Lung Cancer:

2046157532

Source: https://www.industrydocuments.ucsf.edu/docs/qnwl0000

Causes and Prevention. M. Mizell and P. Correa (eds.). Deerfield Beach, Verlag Chimie International, 83-99, 1984.

21. Gillis, C.R., Hole, D.J., Hawthorne, V.M. and Boyle, P., "The Effect of Environmental Tobacco Smoke in Two Urban Communities in the West of Scotland." In: ETS - Environmental Tobacco Smoke: Report from a Workshop on Effects and Exposure Levels. R. Rylander, Y. Peterson and M.-C. Snella (eds.). Published simultaneously in European Journal of Respiratory Disease, Supplement 133, Volume 65, 121-126, 1984.

22. Lam, W.K., A Clinical and Epidemiological Study of Carcinoma of Lung in Hong Kong, M.D. Thesis Submitted to the University of Hong Kong, 1985.

23. Akiba, S., Kato, H. and Blot, W.J., "Passive Smoking and Lung Cancer Among Japanese Women," Cancer Research 46: 4804-4807, 1986.

24. Brownson, R.C., Reif, J.S., Keefe, T.J., Ferguson, S.W. and Pritzl, J.A., "Risk Factors for Adenocarcinoma of the Lung," American Journal of Epidemiology 125(1): 25-34, 1987.

25. Gao, Y.-T., Blot, W.J., Zheng, W., Ershow, A.G., Hsu, C.W., Levin, L.I., Zhang, R. and Fraumeni, J.F., "Lung Cancer Among Chinese Women," International Journal of Cancer 40: 604-609, 1987.

26. Humble, C.G., Samet, J.M. and Pathak, D.R., "Marriage to a Smoker and Lung Cancer Risk," American Journal of Public Health 77(5): 598-602, 1987.

27. Lam, T.H., Kung, I.T.M., Wong, C.M., Lam, W.K., Kleevens, J.W.L., Saw, D., Hsu, C., Seneviratne, S., Lam, S.Y., Lo, K.K. and Chan, W.C., "Smoking, Passive Smoking and Histological Types in Lung Cancer in Hong Kong Chinese Women," British Journal of Cancer 56(5): 673-678, 1987.

28. Pershagen, G., Hrubec, Z. and Svensson, C., "Passive Smoking and Lung Cancer in Swedish Women," American Journal of Epidemiology 125(1): 17-24, 1987.

29. Geng, G.-Y., Liang, T.H., Zhang, A.Y. and Wu, G.L., "On the Relationship Between Smoking and Female Lung Cancer." In: Smoking and Health 1987. M. Aoki, S. Hisamichi and S. Tominaga (eds.). Amsterdam, Excerpta Medica, 483-486, 1988.

30. Inoue, R. and Hirayama, T., "Passive Smoking and Lung Cancer in Women." In: Smoking and Health 1987. M. Aoki, S.

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Source: https://www.industrydocuments.ucsf.edu/docs/qnwl0000

Hisamichi and S. Tominaga (eds.). Amsterdam, Excerpta Medica, 283-285, 1988.

31. Sobue, T., Suzuki, R., Nakayama, N., Inubuse, C., Matsuda, M., Doi, O., Mori, T., Furuse, K., Fukuoka, M., Yasumitsu, T., Kuwabara, O., Ichigaya, M., Kurata, M., Kuwabara, M., Nakahara, K., Endo, S. and Hattori, S., "Passive Smoking Among Nonsmoking Women and the Relationship Between Indoor Air Pollution and Lung Cancer Incidence -- Results of a Multicenter Case Controlled Study," Gan to Rinsho 36(3): 329-333, 1990.

32. Liu, Z., He, X. and Chapman, R.S., "Smoking and Other Risk Factors for Lung Cancer in Xuanwei, China," International Journal of Epidemiology 20(1): 26-31, 1991.

33. Wynder, E.L. and Kabat, G.C., "Environmental Tobacco Smoke and Lung Cancer: A Critical Assessment." In: Indoor Air Quality. H. Kasuga (ed.). Berlin, Heidelberg, Springer-Verlag, 5-15, 1990.

34. Kilpatrick, S., "Misclassification of Environmental Tobacco Smoke Exposure: Its Potential Influence on Studies of Environmental Tobacco Smoke and Lung Cancer," Toxicology Letters 35: 163-168, 1987.

35. Friedman, G., Petitti, D.B. and Bawol, R.D., "Prevalence and Correlates of Passive Smoking," American Journal of Public Health 73(4): 401, 1983.

36. Pron, G.E., Burch, J.D., Howe, G.R. and Miller, A.B., "The Reliability of Passive Smoking Histories Reported in a Case-Control Study of Lung Cancer," American Journal of Epidemiology 127(2): 267-273, 1988.

37. Schenker, M., Hammond, K., Samuels, S., Kado, N. and Woskie, S., "Assessment of Environmental Tobacco Smoke Exposure in Epidemiologic Studies," Chest 91(2): 313-314, 1987. Abstract.

38. Lerchen, M.L. and Samet, J.M., "An Assessment of the Validity of Questionnaire Responses Provided by a Surviving Spouse," American Journal of Epidemiology 123(3): 481-489, 1986.

39. Sandler, D.P. and Shore, D.L., "Quality of Data on Parents' Smoking and Drinking Provided by Adult Offspring," American Journal of Epidemiology 124(5): 768-778, 1986.

40. Leaderer, B., "Assessing Exposures to Environmental Tobacco Smoke," Risk Analysis 10(1): 19-26, 1990.

2046157534

Source: https://www.industrydocuments.ucsf.edu/docs/qnwl0000

41. Shimizu, Y., Namekata, T. and Takemoto, K., "Epidemiological Issues on Involuntary Smoking and Lung Cancer." In: Indoor Air Quality. H. Kasuga (ed.). Berlin, Heidelberg, Springer-Verlag, 323-332, 1990.

42. National Research Council, National Academy of Sciences, "Current and Anticipated Applications." In: Human Exposure Assessment for Airborne Pollutants: Advances and Opportunities. Washington, D.C., National Academy Press, 207-218, 1991.

43. Wynder, E. "Guidelines to the Epidemiology of Weak Associations," Preventive Medicine 16: 211-212, 1987.

44. Wynder, E. and Kabat, G., "Health Care and Society: Environmental Tobacco Smoke and Lung Cancer." In: Present and Future of Indoor Air Quality. C. Bieva, Y. Courtois and M. Govaerts (eds.). Amsterdam, Elsevier Science Publishers, 135-145, 1989.

45. Faccini, J.M., "The Role of Histopathology in the Evaluation of Risk of Lung Cancer from Environmental Tobacco Smoke," Experimental Pathology 37: 177-180, 1989.

46. Katzenstein, A., Environmental Tobacco Smoke (ETS) and Risk of Lung Cancer -- How Convincing is the Evidence?, Larchmont, New York, Katzenstein Associates, March, 1987.

47. Mantel, N., "Lung Cancer and Passive Smoking," British Medical Journal 294: 440, 1987.

48. Lee, P., "Deaths in Canada from Lung Cancer Due to Involuntary Smoking," CMAJ 137: 372-373, 1987.

49. Gordis, L., "Challenges to Epidemiology in the Next Decade," American Journal of Epidemiology 128(1): 1-9, 1988.

50. Newcombe, R.G., "Towards a Reduction in Publication Bias," British Medical Journal 295: 656-659, 1987.

51. Buffler, P.A., "The Evaluation of Negative Epidemiologic Studies: The Importance of All Available Evidence in Risk Characterization," Regulatory Toxicology and Pharmacology 9: 34-43, 1989.

52. Lee, P., "Passive Smoking and Lung Cancer: Problems in Interpreting the Epidemiological Data," Presentation to the Toxicology Forum, Washington, D.C., February, 1987.

2046157535

Source: https://www.industrydocuments.ucsf.edu/docs/qnwl0000

53. Lee, P., "Does Breathing Other People's Tobacco Smoke Cause Lung Cancer?," British Medical Journal 293: 1503-1504, 1986.

54. Lee, P., "Misclassification as a Factor in Passive Smoking Risk," Lancet 2(8511): 867, 1986.

55. Lee, P., "Lung Cancer and Passive Smoking: Association or Artefact Due to Misclassification of Smoking Habits?," Toxicology Letters 35: 157-162, 1987.

56. Lee, P., "Passive Smoking and Lung Cancer Association: A Result of Bias?," Human Toxicology 6: 517-524, 1987.

57. Lee, P., "An Alternative Explanation for the Increased Risk of Lung Cancer in Non-Smokers Married to Smokers." In: Indoor and Ambient Air Quality. R. Perry and P. Kirk (eds.). London, Selper Ltd., 149-158, 1988.

58. Lee, P., "Passive Smoking and Lung Cancer: Fact or Fiction?" In: Present and Future of Indoor Air Quality. C. Bieva, Y. Courtois and M. Govaerts (eds.). Amsterdam, Elsevier Science Publishers, 119-128, 1989.

59. Lee, P.N., "Increased Risk of Lung Cancer in Non-Smokers Married to Smokers: A Result of ETS Exposure or of Bias?," In: Indoor Air Quality. H. Kasuga (ed.). Berlin, Heidelberg, Springer-Verlag, 25-36, 1990.

60. Katzenstein, A.W., "An Estimate of Adult Mortality in the United States from Passive Smoking: A Response," Environment International 16: 175-178, 1990.

61. Rylander, R., "Environmental Tobacco Smoke and Lung Cancer," The New England Journal of Medicine 323(12): 834, 1990.

62. Chen, B.H., Hong, C.J., Pandey, M.R. and Smith, K.R., "Indoor Air Pollution in Developing Countries," World Health Statistics Quarterly 43: 127-138, 1990.

63. Anonymous, "Indoor Air Pollution in Developing Countries," Lancet 336(8730): 1548, 1990.

64. deSerres, F. and Matsushima, T., "Meeting Report: Mutagenesis and Carcinogenesis by Nitropyrenes and Cancer Chemotherapeutics," Mutation Research 164: 4, 1986.

65. Anonymous, "Lung Cancer in South China," Oncology Times, 8(6): 33, 1986.

2046157536

Source: https://www.industrydocuments.ucsf.edu/docs/qnwl0000

66. He, X., Chen, W., Liu, Z. and Chapman, R.S., "An Epidemiological Study of Lung Cancer in Xuan Wei County, China: Current Progress," Archives of Environmental Health 46(2): 118-119, 1991. Abstract.

67. Mumford, J.L., He, X.Z., Chapman, R.S., Cao, S.R., Harris, D.B., Li, X.M., Xian, Y.L., Jiang, W.Z., Xu, C.W., Chuang, J.C., Wilson, W.E. and Cooke, M., "Lung Cancer and Indoor Air Pollution in Xuan Wei, China," Science 235: 217-220, 1987.

68. Chapman, R.S., Mumford, J.L., Harris, D.B., He, X., Jiang, W. and Yang, R., "The Epidemiology of Lung Cancer in Xuan Wei, China: Current Progress, Issues and Research Strategies," Archives of Environmental Health 43(2): 180-185, 1988.

69. Wang, F.-L., et al., "Analysis of Risk Factors for Female Lung Cancer in Haerbin: Indoor Air Pollution," Chinese Journal of Preventive Medicine 23(5): 270-273, 1989.

70. Du, Y.-X. and Ou, X.-L., "Indoor Air Pollution and Woman Lung Cancer." In: Indoor Air '90: Proceedings of the 5th International Conference on Indoor Air Quality and Climate. Toronto, Canada, Volume 1, 59-64, July 29-August 3, 1990.

71. He, F., "Health Effects of Indoor Air Pollution by Coal Combustion in China." In: Indoor Air Quality and Ventilation. London, Selper, Ltd., 305-311, 1990.

72. Xu, Z.-Y., Blot, W.J., Xiao, H.-P., Wu, A., Feng, Y.-P., Stone, B.J., Sun, J., Ershow, A.G., Henderson, B.E. and Fraumeni, J.F., "Smoking, Air Pollution, and the High Rates of Lung Cancer in Shenyang, China," Journal of the National Cancer Institute 81: 1800-1806, 1989.

73. Bu, W., "Ventilation and Its Effects on Pollution in Chinese Kitchens." In: Indoor Air Quality and Ventilation. London, Selper, Ltd., 129-132, 1990.

74. Bazas, B., "An Overview of Indoor Air Quality in Certain Greek Industries, Workshops and Offices." In: Indoor Air Quality and Ventilation. London, Selper, Ltd., 237-240, 1990.

75. Koo, L.C., Ho, J.H.-C. and Rylander, R., "Life-History Correlates of Environmental Tobacco Smoke: A Study on Nonsmoking Hong Kong Chinese Wives with Smoking Versus Nonsmoking Husbands," Soc Sci Med 26(7): 751-760, 1988.

76. Koo, L., "Dietary Habits and Lung Cancer Risk Among Chinese Females in Hong Kong Who Never Smoked," Nutrition and Cancer 11: 155-172, 1988.

2046157537

Source: https://www.industrydocuments.ucsf.edu/docs/qnwl0000

77. Koo, L.C., "Environmental Tobacco Smoke and Lung Cancer: Is It the Smoke or the Diet?" In: Present and Future of Indoor Air Quality. C.J. Bieva, Y.Courtois and M. Govaerts (eds.). Amsterdam, Elsevier Science Publishers, 65-75, 1989.

78. Koo, L.C. and Ho, J.H.-C., "Is There a Threshold Effect for ETS? Results of Data from Chinese Females Who Had Never Smoked." In: Indoor Air Quality. H. Kasuga (ed.). Berlin, Heidelberg, Springer-Verlag, 290-298, 1990.

79. Sidney, S., Cann, B.J. and Friedman, G.D., "Daily Intake of Carotene in Nonsmokers With and Without Passive Smoking at Home," American Journal of Epidemiology 129(6): 1305-1309, 1989.

80. Le Marchand, L., Wilkens, L.R., Hankin, J.H. and Haley, N.J., "Dietary Patterns of Female Nonsmokers With and Without Exposure to Environmental Tobacco Smoke," Cancer Causes and Control 2: 11-16, 1991.

81. Waller, K.D. and Smith, A.H., "Effects of Socioeconomic Status and Smoking on Serum Beta-Carotene," Archives of Environmental Health 46(2): 120, 1991.

82. Tewes, F.J., Koo, L.C., Meisgen, T.J. and Rylander, R., "Lung Cancer Risk and Mutagenicity of Tea," Environmental Research 52: 23-33, 1990.

83. Rylander, R. and Koo, L.C., "Environmental Tobacco Smoke and Lung Cancer -- Recent Aspects on Confounders and Dose Levels." In: Indoor Air Quality. H. Kasuga (ed.). Berlin, Heidelberg, Springer-Verlag, 133-137, 1990.

84. Sterling, T., Weinkam, J. and Sterling, D., "Exposure of Homemakers to Toxic Contaminants: I. Differences in Chronic Conditions Between Homemakers and Employed Persons." In: Indoor Air '90: Proceedings of the 5th International Conference on Indoor Air Quality and Climate. Toronto, Canada, Volume 1, 471-476, July 29-August 3, 1990.

85. Holst, P.A., Kromhout, D. and Brand, R., "For Debate: Pet Birds as an Independent Risk Factor for Lung Cancer," British Medical Journal 297: 1319-1321, 1988.

86. Gori, G.B. and Mantel, N., "Mainstream and Environmental Tobacco Smoke," Regulatory Toxicology and Pharmacology 14: 88-105, 1991.

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Response to Question 2a(iii) (continued):

Heart Disease

The following material discusses and provides references to articles from the literature on heart disease and "passive" tobacco smoke (PTS) which have some potential relevance to workplace exposure. There are very few epidemiological data explicitly based on the workplace. However, there are some preliminary data and speculations. In addition, a number of epidemiological studies and reviews, although not specifically relating to the workplace, nevertheless provide information on the more general issue of a potential relationship between PTS exposure and heart disease. There are scientific uncertainties in attempting to use this literature to draw conclusions concerning the narrower issue of the workplace. Taken together, however, the available epidemiological data do not adequately support a conclusion that PTS causes heart disease in nonsmokers.

In addition to the epidemiologic data, this submission also discusses related literature that may impinge on the scientific basis for claims concerning PTS and heart disease. Some articles comment on the cardiovascular implications of the extremely low levels of PTS or carbon monoxide to which nonsmokers might be exposed. Other articles relate to the general question of what acute effects (e.g., on heart rate, blood pressure or exercise

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performance) PTS might have on the cardiovascular system in either healthy subjects or angina patients. Articles along similar lines, but which relate to carbon monoxide (CO), are also included, in view of the importance CO is sometimes considered to have in cardiovascular function. Due to the scope of the literature on these points, the references cited are not comprehensive. However, they are representative of questions raised in the literature about facets of cardiovascular function that have been sometimes claimed to be related to heart disease in PTS-exposed nonsmokers. Overall, these materials point to a number of inadequacies in the scientific argument that PTS exposure is a cause of heart disease.

These following discussions and citations are organized according to whether they focus on: epidemiological reports of original data or reviews; exposure levels of PTS or carbon monoxide; and healthy subjects or "compromised" individuals (typically angina patients). Accordingly, the specific organization is as follows:

Epidemiology

Primary epidemiological reports..... p. 3

Epidemiological reviews claiming PTS-associated risk..... p. 9

Epidemiological reviews challenging claims of PTS-associated risk..... p. 12

Comments generally emphasizing the low levels of PTS constituents, especially carbon monoxide..... p. 15

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Acute effects

PTS exposure -- healthy subjects..... p. 20

PTS or CO exposure -- angina patients and other compromised individuals..... p. 26

Epidemiology

Primary epidemiological reports

None of the epidemiological studies which have examined workplace smoking in relation to heart disease have reported a statistically significant relationship of such exposure with heart disease. Only five studies commented substantively on some aspect of workplace exposure.[1 2 3 4 5] Three of these provided workplace exposure estimates.[1 4 5] All three were consistent in not reporting a relationship of such exposure with heart disease. The other two studies[2 3] briefly addressed the workplace smoking issue but did not provide data on a possible association with heart disease. One of these studies merely provided an estimate of workplace exposure.[3] The other speculated that unmeasured workplace exposure might have influenced the estimates of PTS risk associated with household exposure.[2] Accordingly, to the extent that actual data are available on workplace smoking, the literature does not suggest a basis for claims that workplace PTS exposure is related to heart disease in nonsmokers.

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The five epidemiological studies which comment on workplace exposure are described more fully below.

Dobson, A.J., Alexander, H.M., Heller, R.F. and Lloyd, D.M. (1991)[1]

This article provides epidemiological data concerning a potential relationship between environmental tobacco smoke exposure and heart disease. All subjects were residents of the Hunter region of New South Wales, Australia. It used a case-control design. The cases were all individuals, male or female, within that region who experienced a "fatal or non-fatal definite or possible myocardial infarction or a coronary death." The controls were a sample comprising individuals in this region who were participating in an ongoing risk factor prevalence study sponsored by the World Health Organization. Data were collected on certain demographic characteristics, medical history, cigarette smoking and PTS exposure at home and work.

Odds ratios and 95% confidence intervals reported for heart disease risk associated with PTS exposure at home were 0.97 (0.50-1.86) for men and 2.46 (1.47-4.13) for women. For PTS exposure at work, the odds ratios and confidence intervals were 0.95 (0.51-1.78) for men and 0.66 (0.17-2.62) for women. The authors concluded that the "odds ratios for passive smoking at work did not suggest increased risk."

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Although the authors expressed a belief that their study supports an adverse effect of both smoking and PTS exposure at home, they commented on a variety of sources of biases in their study, including potential effects of confounding. "On balance, the effects of bias and confounding could have led to overestimation of risks due to passive and active smoking."

Helsing, K.J., Sandler, D.P., Comstock, G.W. and Chee, E. (1988)[2]

This report provides data on a 12-year follow-up of a Washington County, Maryland, population, and is based on information concerning household exposure. There are no workplace data. However, the authors commented on the potential influence on their results of presumed exposure at work and elsewhere outside the home. They suggested that "some of those presumed to have zero or moderate exposure at home were actually subjected to moderate or heavy passive smoke at work or elsewhere outside the home." (p. 921) This exposure would mean there was no true no-exposure control, and accordingly, it would weaken the apparent association of household smoke exposure with heart disease mortality. In this study, only about one-half of the women worked outside the home. However, almost all of the men worked outside of the home.

This may in part explain the greater consistency over age groups among women than among men in

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the increase in relative risk with indicated level of exposure. (p. 921)

It bears emphasis that these comments on workplace smoking reflect opinions of the authors. They are not descriptive of data, and, accordingly, should be considered as speculation.

Hirayama, T. (1984)[3]

PTS exposure was assessed via husbands' smoking, and there are no explicit workplace data. However, ischemic heart disease (i.e., related to constriction or obstruction of a blood vessel) mortality rates in women are broken down according to age, occupation and smoking habit of the husband. Hirayama also mentioned that he had performed a survey which provided data on exposure in the workplace. He stated:

> Our recent survey showed that 47.5% and 32.6% of Japanese adult women were being exposed to passive smoking at home and at the workplace, respectively. (p. 186)

Also, on page 194, Table 11, point 2, there is a reference to workplace exposure.

Despite these scattered comments regarding PTS workplace exposure, Hirayama does not provide any data concerning any

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estimate of workplace exposure in relation to heart disease incidence.

Lee, P.N., Chamberlain, J. and Alderson, M.R. (1986)[4]

This study provides a small amount of workplace exposure information. Spousal smoking was the primary method of assessing PTS exposure. However, in addition to this basic spousal smoking measurement, there was a questionnaire which asked the subjects to quantify, on a four point scale, the extent to which they were regularly exposed to tobacco smoke in four situations: at home, at work, during daily travel and during leisure time. Table IV, p. 101, presents data on lung cancer, with no evidence of association of any of these indices, including workplace exposure, with lung cancer. Table V, p. 102, gives similar data, summarizing all four indices with regard to heart disease. There is no evidence of an association.

It should be noted that Lee, et al. did report that there was an approximate two-fold increase in stroke risk among people who scored high on the combined PTS exposure index. However, this was not statistically significant.

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Svendsen, K.H., Kuller, L.H., Martin, M.J. and Ockene, J.K. (1987)[5]

This study used smoking status of the wife as an index of PTS exposure. However, a small amount of information was collected regarding the workplace.

> Only a limited amount of information was collected about exposure to tobacco smoke on the job. Participants were asked the smoking status of their coworkers. (p. 785, col. 2)

The following data regarding workplace exposure to PTS were described, indicating no statistically significant association with heart disease.

> Of 1,237 never smokers, 906 (73.2 per cent) reported that most coworkers were smokers, and 331 (26.8 per cent) reported that most coworkers were nonsmokers. The relative risk for the endpoint death from any cause, for men whose coworkers smoked compared with men whose coworkers did not smoke, adjusted for age and wife's smoking status is 1.2 (p = 0.63, 95 per cent CI 0.5-1.8). For the endpoint coronary heart disease death, the relative risk is 2.6 (p = 0.23, CI 0.25-12.7), and for fatal or nonfatal coronary heart disease event, the relative risk is 1.4 (p = 0.26, CI 0.8-2.5).
>
> Because of the small number of deaths, the joint impact of a spouse who smoked and coworkers who smoked was estimated only for the endpoint fatal or nonfatal coronary heart disease event. The risks for the categories wife and coworkers who smoked, wife who smoked and coworkers who did not smoke, and coworkers who smoked and wife who did not smoke relative to the category wife and coworkers who did not smoke are 1.7 (p = 0.14, 95 per cent CI 0.8-

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3.6), 1.2 (p = 0.75, 95 per cent CI 0.4-3.7), and 1.0 p = .99, 95 per cent CI 0.5-1.9), respectively. (p. 791)

Epidemiological reviews claiming PTS-associated risk

Some reviews of the epidemiological literature on PTS and heart disease conclude that a relationship has been established.[6 7 8 9 10] However, only one of these, a paper by Kawachi, et al.,[7] makes an explicit claim that PTS is associated with workplace deaths. The other reviews, nevertheless, make it clear that they believe a general association of PTS with heart disease also applies to the workplace. Because these reviews do not actually provide measurements or estimates of workplace PTS exposure in relation to heart disease, it is arguable that they are not informative on this issue. However, the thrust of these reviews, as they might apply to the workplace, is summarized briefly below.

Wells, A.J. (1988)[6]

Wells' estimate of 46,000 annual PTS-related deaths (32,000 from heart disease) is based on exposure assumptions that include the workplace. For example, it was assumed that a percentage of nonsmokers (whether or not living with a smoker) would nevertheless have some exposure at home or at work. (p. 250, col. 2) Even so, Wells does comment, in discussing lung cancer

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mortality, that the relative risks "are based largely on home exposure." (p. 257, col. 1)

Kawachi, I., Pearce, N.E. and Jackson, R.T. (1989)[7]

These authors specifically estimate workplace PTS exposure for New Zealanders.

> The prevalence of exposure to passive smoking in the workplace has been estimated to be 33.6% and 23.4% for never smoking men and women respectively. (p. 337, col. 1, Abstract)

Relative risks and annual deaths from heart disease were calculated in relation to this estimated exposure.

> The number of ischaemic heart disease deaths due to passive smoking in the workplace was even higher [than for lung cancer], at 152 (range: 62-224), assuming relative risks of 2.3 (CI 1.4-3.4) and 1.9 (CI 1.4-2.5) for men and women respectively. (p. 337, col. 1, Abstract)

It should be emphasized that these claims of heart disease deaths related to workplace PTS exposure are not based on data--that is, not on the observation of heart disease deaths in nonsmokers exposed to PTS at the workplace. Rather, these claimed heart disease deaths are what would theoretically be predicted based on a certain estimated level of overall PTS exposure in the

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population and given the presumption that a certain level of risk stems from such exposure.

Kristensen, T.S. (1989)[8]

The general context of this review's discussion of "passive smoking" is as a potential factor in workplace-related cardiovascular disease. The review, however, does not introduce any new data or assumptions regarding workplace exposure.

Glantz, S.A. and Parmley, W.W. (1991)[9]

Glantz and Parmley acknowledge that their analysis is based on household smoking studies. However, they addressed the workplace issue by citing data that detectable levels of blood cotinine are found in nonsmokers who say they live with nonsmokers, thus "indicating that they are actually exposed to ETS, either at work or at home." (p. 3, col. 2) This type of misclassification, according to the authors, was said to lead to underestimating the PTS-related risk.

According to Glantz and Parmley, relying on household studies also leads to an underestimate of overall risk because workplace PTS exposure tends to be relatively higher than household exposure.

Last, and of note, all these studies are based on the smoking habits of the nonsmoker's spouse

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and, therefore, the exposure to ETS at home. Household exposures to ETS at home are generally much smaller than exposures at work, where the density of smokers is generally higher. As a result, these studies generally underestimate the risk and attendant public health burden due to ETS-induced heart disease. Kawachi et al. adjusted Wells' relative risks to account for workplace exposures to ETS and found that the relative risks increase to 2.3 (95% CI, 1.4-3.4) for men and 1.9 (95% CI, 1.4-2.5) for women. Thus, any potential confounding of the results because of exposure to ETS outside the home will tend to produce underestimates rather than overestimates of the effect of ETS. Likewise, estimates of public health impact based on risks computed from household exposures will be lower than the true public health impact. (p. 4, col. 1)

Steenland, K. (1992)[10]

This article reviews epidemiological and experimental literature related to the claim that PTS causes heart disease. It also calculates an estimate of the number of annual U.S. heart disease deaths attributable to PTS exposure. Although the author, Kyle Steenland, is affiliated with the National Institute for Occupational Safety and Health, his risk assessment is not directed toward potential occupational PTS exposure. Instead, he focuses on nonsmokers' potential PTS exposure at home, as inferred from living with a current or former smoker. Steenland's calculations reflected an "adjustment" for potential PTS exposure outside the home (such as at work or in other social settings). However, this adjustment was based on assumptions about workplace PTS exposure. No data were reported on actual PTS exposures in the workplace or

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even of surrogate measures that might be used to infer PTS exposure. In fact, Steenland acknowledged "the lack of data on exposures to ETS outside the home." (p. 95)

Epidemiological reviews challenging claims of PTS-associated risk

The literature contains several literature reviews which conclude that a potential relationship of PTS exposure and heart disease has not been established.[11] [12] [13] [14] [15] [16] [17] In view of the highly limited data on workplace PTS exposure, it is not surprising that none of these reviews provide conclusions specifically focusing on the workplace. However, these reviews do address broad problems with the PTS/heart disease data. If such data are generally inconclusive, then they are reasonably viewed as also specifically inconclusive in regard to the workplace.

U.S. Department of Health and Human Services (1986)[11]

This review examined the available data and judged that "no firm conclusion" (p. 10) could be made regarding a possible relationship between PTS and heart disease.

Committee on Passive Smoking, Board on Environmental Studies and Toxicology (1986)[12]

This committee report calculated that any potential heart disease risk related to PTS would be "difficult to detect or estimate reliably" from epidemiological studies, and would be "the

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same order of magnitude as what might arise from expected residual confounding due to unmeasured covariates." (p. 263)

Wexler, L.M. (1990)[13]

At the PTS conference held at McGill University in 1989, Lawrence Wexler, of the New York Medical College, concluded that recent data did not provide a basis for altering the earlier conclusions by the Surgeon General and National Research Council concerning PTS and cardiovascular disease.

> Based on the available evidence, it is this author's opinion that it has not been demonstrated that exposure to ETS increases the risk of cardiovascular disease. (p. 139)

Weetman, D.F. and Munby, J. (1990)[14]

Two scientists from the United Kingdom reviewed the literature on PTS and heart disease and presented their conclusions at an international conference on indoor air quality held in Lisbon, Portugal in April 1990.

> It is concluded that no increased risk of cardiovascular disease can be associated unequivocally with exposure to ETS, and it seems probable that this will continue to be the case until specifically designed trials are instigated, and some objective measure of degree of exposure can be devised. (p. 215)

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Thiery, J. and Cremer, P. (1990)[15]

Two physicians from the University of Munich, Germany, presented their conclusions at an international conference in Hungary in June 1990.

> Taking into account the small increase in coronary risk in passive smokers as compared to non-exposed subjects and also the low validity and small number of epidemiological studies available and the fact that their results are at least inconsistent, a relationship between passive smoking and cardiovascular diseases cannot be established on these data. (p. 6)

Armitage, A.K. (1991)[16]

In a 1991 book discussing a wide range of issues involving PTS, the literature on heart disease was reviewed by Alan Armitage, former director of toxicology of a major European research laboratory and now head of pharmacology at the Tobacco Research Council Laboratories in the United Kingdom. He judged that the scientific data have not established an increased heart disease risk in nonsmokers exposed to PTS.

> It is clear that the evidence for a harmful effect of ETS in enhancing CHD [coronary heart disease] risk in non-smokers is not very convincing. . . . (p. 114)

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Lee, P.N. (1991)[17]

> Although it has been demonstrated above that the risk assessment for heart disease essentially rests on the results from two studies, both of which seem unreliable, a number of other general points can be made. First, there are a very large number of risk factors for heart disease. It is evident that adjustment for these factors in the studies has always been incomplete, and often seriously incomplete. Second, the extent of the association seen in some of these studies, which in some cases is close to that reported in relation to active smoking, is implausibly high when viewed against the extent of the association seen in relation to active smoking. Third, there is a major danger of publication bias. It is notable that the literature is still relatively sparse despite the numerous ongoing studies of heart disease and the fact that heart disease in a non-smoker is probably 50 times or so more common than lung cancer in a non-smoker. (p. 200)

Comments generally emphasizing the low levels of PTS constituents, especially carbon monoxide

One way to approach the question of PTS and heart disease is to examine the levels of PTS to which nonsmokers might be exposed. Reported levels of exposure to carbon monoxide may be particularly of interest in view of the potential role some authors have speculated it to have in heart disease. The literature provides many examples of reviews concluding that potential nonsmoker PTS or CO exposure levels are extremely low and not likely to be of physiological significance. The conclusions of several notable examinations of this issue are extracted below.

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Adlkofer, F.X., Scherer, G., Von Meyerinck, L., Von Maltzan, Ch. and Jarczyk, L. (1989)[18]

> COHb in passive smokers rises only slightly above the normal physiological level so that it is difficult to differentiate from COHb-values measured in non-exposed non-smokers. (p. 185)

Cole, P. (1981)[19]

> Another source of CO is the inhalation of exhaled tobacco smoke and sidestream smoke from other smokers, called 'passive smoking'. In a City office adjacent to Barts, where smoking was allowed, we measured the COHb levels in 100 non-smokers working alongside active smokers. Again, the mean level was slightly up, 1.12%, but again the increase is hardly significant. Passive smoking, although undeniably unpleasant to some can hardly be described as a health hazard. The rise in COHb does not even approach that found in an active smoker. In the same City office we measured COHb in a 100 active smokers at the same time. They showed a mean level of 5.5% with a maximum of 13%, a completely different picture. We have rarely found a known non-smoker to exceed a level of 2.5% COHb and most are much lower. (p. 76)

Gori, G.B. and Mantel, N. (1991)[20]

> The daily levels of cigarette consumption compatible with no significantly increased risk for other diseases associated with active smoking appear to be of the same order as for lung cancer. Tables 4 and 5 report the analogous estimates for cardiovascular and respiratory disease mortality, with the implication that retained doses of ETS are unlikely to be associated with significant risk elevations for such disease as well. (p. 96)

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Table 4 in the paper summarizes data from epidemiologic studies of smoking and heart disease, and provides the "maximum levels of daily cigarette consumption at which risk for coronary heart disease mortality in male smokers may not be significantly increased from the risk of nonsmokers." The maximum levels are in the range of 1.5-4.5 cigarettes per day. By contrast, Gori and Mantel calculate that the average PTS-exposure for a nonsmoker is "less than one cigarette over the course of 1 year."

> Together, these considerations suggest that the lung cell doses for average ETS-exposed nonsmokers are probably between 1/10,000 and 1/100,000 of equivalent cell doses for average mainstream active smokers. In practical terms, this implies an annual retained dose of tobacco smoke components equivalent to far less than the dose from the active smoking of one cigarette somehow evenly dispersed over a 1-year period. (p. 94)

Malmfors, T., Thorburn, D. and Westlin, A. (1989)[21]

This is a study of the air quality in passenger aircraft, focusing on components related to PTS. Although no potential health effects were measured, the report emphasizes the low levels of PTS-related components, and observes these are unlikely to have an important cardiovascular significance. It is also noted that the nicotine and carbon monoxide levels in aircraft cabins are well below the standards set by OSHA.

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It can be seen that the nicotine concentrations found in the present study are roughly one-tenth of the standard for the working environment set by OSHA. The concentration of carbon monoxide is also about one-tenth of the standard for general indoor air and even less for the working environment. (p. 623)

From this comparison it appears that the quality of the aircraft cabin air in the present study is satisfactory and better for factors related to ETS - nicotine and carbon monoxide - than for carbon dioxide and relative humidity. (p. 624)

Any effects on the cardiovascular system would have been mostly unnoticed in healthy individuals, because there are no known direct effects of ETS on the cardiovascular system beyond the formation of carboxyhemoglobin. The latter is so minimal that it will not affect the cardiovascular function. (p. 626)

Proctor, C.J., Warren, N.D., Bevan, M.A.J. and Baker-Rogers, J. (1991)[22]

It seems that the main factor in exposure to environmental tobacco smoke is living with a smoker. Exposure at work, leisure, or travel seems to be minor. Overall, exposure to airborne nicotine was found to be low (mean 2.3 $\mu g\ m^{-3}$, median $<0.1\ mg\ m^{-3}$). (p. 296)

Rylander, R. (1983)[23]

The unimportance of carbon monoxide has been further confirmed. . . . CO from ETS is not important from a health point of view. (p. 144)

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Schievelbein, H. and Richter, F. (1984)[24]

> Cardiovascular effects of tobacco smoke have been studied in passive smokers far less extensively than in active smokers. Under real-life conditions, passive smokers inhale approximately 0.02 to 0.01 of the amount of particulate matter taken up by active smokers. Their nicotine concentration in serum is within a range that is barely distinguishable from the background level. The increase in carboxyhemoglobin rarely exceed 1%. In healthy subjects heavily exposed to tobacco smoke, no or only slightly acute effects on the cardiovascular system are found. Whether or not passive smoking is likely to aggravate symptoms in patients with advanced coronary heart disease has not yet been unequivocally established and requires further investigation. From a few studies on occupational groups exposed to carbon monoxide (CO) and from experiments with animals chronically treated with CO or nicotine, the conclusion can be drawn that neither CO nor nicotine is likely to play a role in the development and progression of coronary heart disease in those concentrations normally found in passive smokers. (p. 626)

Acute Effects

PTS exposure -- healthy subjects

Several aspects of cardiovascular function, such as heart rate and blood pressure, can be readily measured in laboratory studies. Even if short-term changes in such parameters were consistently reported following acute exposure to PTS or CO, their potential clinical significance is highly uncertain. On the other

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hand, if the literature does not consistently report important acute cardiovascular responses, this further undermines claims of a potential relationship between PTS and heart disease.

A number of studies and reviews have examined potential acute cardiovascular responses to either PTS or CO. A sample of this literature is cited below, indicating a sizeable body of scientific data and opinion questioning a role of PTS or CO in such effects.

Committee on Passive Smoking, Board on Environmental Studies and Toxicology (1986)[25]

The report reviews studies of possible acute effects of ETS on the cardiovascular system in healthy subjects, and concludes that there are no significant changes. The report, although avoiding a firm conclusion, does express that, for angina patients, there is a possible cause for concern about exposure to the CO in PTS.

> In summary, for normal young adult males and females, no significant acute effects of ETS exposure on heart rate or blood pressure have been reported, either under resting or aerobic conditions. (p. 260)

Fischer, T., Weber, A. and Grandjean, E. (1978)[26]

Potential subjective, irritant and physiological (e.g., heart rate) effects of PTS were assessed in a laboratory setting.

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No pulmonary function or heart rate effects were reported. However, the authors nevertheless consider PTS a serious problem in view of irritant effects, potential effects in sensitive persons and levels to which some restaurant and bar employees are exposed.

> Pulmonary function tests should give us an indication of eventual bronchial constriction, encountered frequently in smokers. In fact, our spirometric methods showed no differences before and after exposure to smoke. The change in heart rate during the test was just as insignificant. (uncertified translation, p. 8)

Harke, H.-P. and Bleichert, A. (1972)[27]

> Measurements of electrocardiogram, blood pressure, and puls [sic] frequency showed, that these parameters were not altered by passive smoking. (p. 312)

Hulka, B.S. (1988)[28]

> Studies of acute ETS exposure in healthy children and adults have shown no statistically significant alterations in heart rate or blood pressure either during resting conditions or during exercise. Studies of ETS exposure in persons with pre-existing atherosclerotic heart disease have been inconclusive. Important questions about ETS exposure and the induction of angina, electrocardiographic abnormalities, and cardiac arythmias are unanswered. (p. 537)

International Collaborative Group (1984)[29]

This study examined children (approximately 13 years old) from cities in Germany, Cuba, Hungary and the USSR. Two sample

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groups were compared, one representing the upper 5% and one representing the remainder of the blood pressure distribution curve. One of the characteristics compared between these two groups was parental smoking habits. No significant association was reported between the children's blood pressure and parental smoking.

> The proportion of smokers among the fathers was slightly higher in the lower (55.8%) than in the upper group (54.7%); this difference was not significant. The proportion of smokers among mothers was, however, significantly higher in the lower than in the upper group ($P<0.01$). The proportion of smoking fathers was lowest in Berlin-Köpenick (46.3% vs. 38.6%) and highest in Havana (66.3% vs. 66.7%). The proportion of smoking mothers was lowest in Moscow 3 (0% vs. 1.4%) and highest in Budapest (29.4% vs. 32.0%). The mean blood pressure values of the children showed no significant association with the smoking habits of either parent. (p. 122)

Pimm, P.E., R.J. Shephard and F. Silverman (1978)[30]

> It is concluded that in normal subjects the magnitude of physiological responses to acute exposures is minimal. . . . (p. 201)

Rummel, R.M., Crawford, M. and Bruce, P. (1975)[31]

Heart rate and blood pressure measurements were made on 17 male and 39 female nonsmoking college students at 5, 10, 15, and 20 minutes during exposure to exhaled cigarette smoke in an

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enclosed room. . . . Measurements were correlated with attitudes toward smoke exposure.

For the entire group of nonsmokers, there were no significant changes in heart rate or diastolic blood pressure during the smoke exposure, but systolic blood pressure was significantly increased at 5 minutes of exposure; at 20 minutes of exposure it had returned to preexposure values.

When results were examined according to nonsmokers attitudes, those who "disliked" being exposed had significantly greater heart rates than those who were "indifferent" at all measurements; blood pressures between the two groups did not differ significantly.

Samet, J.M. (1988)[32]

> While these effects [relating to oxygen transport, heart and blood pressure increases, etc.] of carbon monoxide and nicotine may impair performance, exposures to environmental tobacco smoke are generally at concentrations below which physiological effects would be expected. (p. 12, col. 1)

Shephard, R.J., Collins, R. and Silverman, F. (1979)[33]

The responses of healthy men and women were measured during exercise performance while exposed to PTS vs. a sham exposure. Among several other variables, heart rate was measured.

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During a preexposure period, those subjects who were to undergo PTS exposure had higher heart rates than the sham subjects. However, actual exposure was associated with a smaller heart rate increase compared to the sham condition.

> The heart rate was higher before the experimental than before the sham exposures. . . . However, while actually exposed to the cigarette smoke both the increment of heart rate and the absolute heart rate were less than in the corresponding sham exposure. (p. 285)

The authors suggested that these heart rate changes might be related to a subjective anxiety or hyperventilation reaction, rather than an actual physiological response to PTS.

Weber-Tschopp, A., Fischer, T. and Grandjean, E. (1976)[34]

> Thirtythree subjects were exposed in a climatic chamber to cigarette smoke (side stream) produced by a smoking machine. . . . $\%FEV_1/VC$, MMF and heart rate were not significantly affected during exposure. (p. 277)

Weber, A., Fischer, T. and Grandjean, E. (1979)[35]

> In a first study subjects were exposed for 1 hr to constant cigarette smoke concentrations corresponding to 5 or 10 ppm CO. Annoyance, subjective eye irritations, and eye blink rate increase in both conditions during the first 30 min of exposure. Respiratory frequency and heart rate variability are not altered. (p. 205)

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Winneke, G., Plischke, K., Roscovanu, A. and Schlipkoeter, H.-W. (1984)[36]

> Neither blood pressure-values, nor heart-rates or fingerpulse-volume were influenced by exposure to tobacco-smoke. This correspond to the fact that nicotine-intake from passive smoking is negligible. Depth and rate of breathing were not altered either. (p. 353)
>
> As for carbon monoxide (CO) there was pronounced uptake in terms of COHb for the high exposure-condition only. In absolut terms, however, the measured values correspond to those found in non-smoking urban populations, and are well below levels considered critical for persons with cardio-vascular impairment. (p. 354)

Winneke, G., Neuf, M., Roscovanu, A. and Schlipköter, H.-W. (1990)[37]

Physiological measurements were obtained from nonsmokers, while they were in an exposure chamber in which another individual was smoking. No significant effects were reported for heart rate or blood pressure. The authors reported that "cardiorespiratory variables were not affected by ETS exposure." (p. 173)

> In taking CO as the basis for comparison our cardiovascular findings are consistent with those of others, who, at even higher levels of ETS-exposure did not observe exposure-related increase of either heart-rate or blood-pressure. Nicotine-intake at such ETS-levels is likely to be too low for cardiovascular changes to be expected. (p. 181)

PTS or CO exposure -- angina patients and other compromised individuals

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Claims are sometimes made that PTS, or specifically CO in PTS, aggravates cardiovascular disease in people with pre-existing illness. Such claims typically stem from a limited and largely discredited report by Wilbert Aronow that angina patients experienced chest pain sooner when exercising in the presence of PTS.[38] However, a closer examination of the literature reveals a body of data that raises questions about whether PTS, or CO at levels reported to be in PTS, has significant adverse cardiovascular effects.

Hinderliter, A.L., Adams, K.F., Price, C.J., Herbst, M.C., Koch, G. and Sheps, D.S. (1989)[39]

> In conclusion, low-level CO exposure is not arrhythmogenic in patients with coronary heart disease and no ventricular ectopy at baseline. (p. 89)

McNicol, M.W. and Turner, McM. (1983)[40]

> There was no change in the mean oxygen uptake at the onset of angina with any intervention. . . . These results are in contrast with previous reports of the effects of smoking and carbon monoxide on exercise performance in angina pectoris. However in all of these other studies a subjective rather than objective end point was used. We suggest that an objective assessment is essential and that oxygen uptake at the onset of angina is useful and relatively easy to measure.

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Shephard, R.J., Collins, R. and Silverman, F. (1979)[41]

This study was an attempt to determine if asthmatic subjects have an increased sensitivity to PTS exposure. Respiratory symptoms, pulmonary function and heart rates were measured. Although some slight effects (e.g., a small heart rate increase) were reported, these were considered to be of "doubtful biological importance" and most likely due to an emotional, rather than directly physiological, response to the PTS exposure.

> There was also some evidence of arousal and/or emotional excitement, including a slight tachycardia (at 80-min exposure, $P<0.05$) and a slight increase of forced vital capacity ($P<0.05$ at 90-min exposure). However, dynamic lung volumes . . . were unaltered. . . . Our data thus do not suggest that asthmatic subjects have an unusual sensitivity to cigarette smoke. (p. 392)
>
> The physiological changes observed in normal subjects during smoke exposure, although occasionally reaching conventional levels of statistical significance, were of doubtful biological importance (Pimm et al., 1978; Shephard et al., 1979a). Findings included some increase of heart rate and respiratory minute volume, probably of emotional origin, a tendency of increase in functional residual capacity and residual volume in some experiments, and small decreases of dynamic lung volumes. The asthmatic subjects also showed emotional reactions to the cigarette smoke, including the tachycardia, and possibly the preexposure increase of FRC and TLC. (pp. 399, 401)
>
> We would thus conclude that the specific sensitivity of asthmatic subjects is not a major consideration when determining air quality criteria for rooms contaminated by cigarette smoke. (p. 402)

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Sheps, D.S., Adams, K.F., Bromberg, P.A., Goldstein, G.M., O'Neil, J.J., Horstman, D. and Koch, G. (1987)[42]

In conclusion, there is no clinically significant effect of 3.8% COHb (representing a 2.2% increase from resting values) on the cardiovascular system in this study. (p. 108)

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REFERENCES

1. Dobson, A.J., Alexander, H.M., Heller, R.F. and Lloyd, D.M., "Passive Smoking and the Risk of Heart Attack or Coronary Death," The Medical Journal of Australia 154: 793-797, 1991

2. Helsing, K.J., Sandler, D.P., Comstock, G.W. and Chee, E., "Heart Disease Mortality in Nonsmokers Living With Smokers," American Journal of Epidemiology 127(5): 915-922, 1988.

3. Hirayama, T., "Lung Cancer in Japan: Effects of Nutrition and Passive Smoking." In: Lung Cancer: Causes and Prevention. M. Mizell and P. Correa (eds.). New York, Verlag Chemie International, Chapter 14, 175-195, 1984.

4. Lee, P.N., Chamberlain, J. and Alderson, M.R., "Relationship of Passive Smoking to Risk of Lung Cancer and Other Smoking-Associated Diseases," British Journal of Cancer 54: 97-105, 1986.

5. Svendsen, K.H., Kuller, L.H., Martin, M.J. and Ockene, J.K., "Effects of Passive Smoking in the Multiple Risk Factor Intervention Trial," American Journal of Epidemiology 126(5): 783-795, 1987.

6. Wells, A.J., "An Estimate of Adult Mortality in the United States from Passive Smoking," Environment International 14(3): 249-265, 1988.

7. Kawachi, I., Pearce, N.E. and Jackson, R.T., "Deaths from Lung Cancer and Ischaemic Heart Disease Due to Passive Smoking in New Zealand," New Zealand Medical Journal 102(871): 337-340, 1989.

8. Kristensen, T.S., "Cardiovascular Diseases and the Work Environment. A Critical Review of the Epidemiologic Literature on Chemical Factors," Scand J Work Environ Health 15: 245-264, 1989.

9. Glantz, S.A. and Parmley, W.W., "Passive Smoking and Heart Disease: Epidemiology, Physiology, and Biochemistry," Circulation 83(1): 1-12, 1991.

10. Steenland, K., "Passive Smoking and the Risk of Heart Disease," JAMA 267(1): 94-99, 1992.

11. U.S. Department of Health and Human Services, The Health Consequences of Involuntary Smoking: A Report of the Surgeon General. Publication No. DHHS (CDC) 87-8398, Washington, D.C.,

2046157569

Source: https://www.industrydocuments.ucsf.edu/docs/qnwl0000

U.S. Government Printing Office, 1986.

12. Committee on Passive Smoking, Board on Environmental Studies and Toxicology, National Research Council, National Academy of Sciences, Environmental Tobacco Smoke: Measuring Exposures and Assessing Health Effects. Washington, D.C., National Academy Press, 1986.

13. Wexler, L.M., "Environmental Tobacco Smoke and Cardiovascular Disease: A Critique of the Epidemiological Literature and Recommendations for Future Research." In: Environmental Tobacco Smoke: Proceedings of the International Symposium at McGill University 1989. D.J. Ecobichon and J.M. Wu (eds.). Lexington, Mass., Lexington Books, D.C. Heath and Company, Chapter 8, 139-152, 1990.

14. Weetman, D.F. and Munby, J., "Environmental Tobacco Smoke (ETS) and Cardiovascular Disease." In: Indoor Air Quality and Ventilation. F. Lunau and G.L. Reynolds (eds.). London, Selper Ltd., 211-216, 1990.

15. Thiery, J. and Cremer, P., "Coronary Heart Disease and Involuntary Smoking," Paper presented at: Toxicology Forum (Session on "Environmental Tobacco Smoke: Science and Meta-Science"), Budapest, Hungary, June 19, 1990.

16. Armitage, A.K., "Environmental Tobacco Smoke and Coronary Heart Disease." In: Other People's Tobacco Smoke. A.K. Armitage (ed.). Beverly, E. Yorks, U.K., Galen Press, Chapter 7, 109-116, 1991.

17. Lee, P.N., "Weaknesses in Recent Risk Assessments of Environmental Tobacco Smoke," Environmental Technology 12(3): 193-208, 1991.

18. Adlkofer, F.X., Scherer, G., Von Meyerinck, L., Von Maltzan, Ch. and Jarczyk, L., "Exposure to ETS and its Biological Effects: A Review." In: Present and Future of Indoor Air Quality: Proceedings of the Brussels Conference, 14-16 February 1989. C.J. Bieva, Y. Courtois and M. Govaerts (eds.). New York, Elsevier Science Publishing Company, Inc., 183-196, 1989.

19. Cole, P., "Smoking Habits and Carbon Monoxide." In: Smoking and Arterial Disease, R.M. Greenhalgh (ed.). Pittman Medical, Chapter 10, 74-83, 1981.

20. Gori, G.B. and Mantel, N., "Mainstream and Environmental Tobacco Smoke," Regulatory Toxicology and Pharmacology 14: 88-105, 1991.

2046157570

Source: https://www.industrydocuments.ucsf.edu/docs/qnwl0000

21. Malmfors, T., Thorburn, D. and Westlin, A., "Air Quality in Passenger Cabins of DC-9 and MD-80 Aircraft," Environmental Technology Letters 10: 613-628, 1989.

22. Proctor, C.J., Warren, N.D., Bevan, M.A.J. and Baker-Rogers, J., "A Comparison of Methods of Assessing Exposure to Environmental Tobacco Smoke in Non-Smoking British Women," Environment International 17: 287-297, 1991.

23. Rylander, R., "Workshop Perspectives." In: ETS--Environmental Tobacco Smoke. Report from a Workshop on Effects and Exposure Levels, R. Rylander, Y. Peterson and M.-C. Snella (eds.). Chapter 5, 143-145, University of Geneva, Switzerland, March 15-17, 1983.

24. Schievelbein, H. and Richter, F., "The Influence of Passive Smoking on the Cardiovascular System," Preventive Medicine 13: 626-644, 1984.

25. Committee on Passive Smoking, Board on Environmental Studies and Toxicology, National Research Council, National Academy of Sciences, Environmental Tobacco Smoke: Measuring Exposures and Assessing Health Effects. Washington, D.C., National Academy Press, 1986.

26. Fischer, T., Weber, A. and Grandjean, E., "Extent and Effect of Air Pollution by Tobacco Smoke Under Experimental Conditions and in Restaurants," (translated from German), Schweiz Blatt Luft 45: 3-8, 1978.

27. Harke, H.-P. and Bleichert, A., "On the Problem of Passive Smoking," Int Arch Arbeitsmed 29: 312-322, 1972.

28. Hulka, B.S., "The Health Consequences of Environmental Tobacco Smoke," Environmental Technology Letters 9: 531-538, 1988.

29. International Collaborative Group, "International Collaborative Study on Juvenile Hypertension. 2. First Follow-Up Report," Bulletin of the World Health Organization 62(1): 121-132, 1984.

30. Pimm, P.E., R.J. Shephard and F. Silverman, "Physiological Effects of Acute Passive Exposure to Cigarette Smoke," Archives of Environmental Health 33(4): 201-213, 1978.

31. Rummel, R.M., Crawford, M. and Bruce, P., "The Physiological Effects of Inhaling Exhaled Cigarette Smoke in Relation to Attitude of the Nonsmoker," The Journal of School Health 45(9): 524-529, 1975.

2046157571

Source: https://www.industrydocuments.ucsf.edu/docs/qnwl0000

32. Samet, J.M., "Involuntary Exposure to Tobacco Smoke," Annals of Sports Medicine 4(1): 1-15, 1988.

33. Shephard, R.J., Collins, R. and Silverman, F., "Responses of Exercising Subjects to Acute 'Passive' Cigarette Smoke Exposure," Environmental Research 19: 279-291, 1979.

34. Weber-Tschopp, A., Fischer, T. and Grandjean, E., "Physiological and Psychological Effects of Passive Smoking," (translated from German), Int. Arch. Occup. Environ. Hlth. 37(4): 277-288, 1976.

35. Weber, A., Fischer, T. and Grandjean, E., "Passive Smoking in Experimental and Field Conditions," Environmental Research 20(1): 205-216, 1979.

36. Winneke, G., Plischke, K., Roscovanu, A. and Schlipkoeter, H.-W., "Patterns and Determinants of Reaction to Tobacco Smoke in an Experimental Exposure Setting." In: Indoor Air: Radon, Passive Smoking, Particulates and Housing Epidemiology. B. Berglund, T. Lindvall and J. Sundell (eds.). Vol. 2, 351-356, 1984.

37. Winneke, G., Neuf, M., Roscovanu, A. and Schlipköter, H.-W., "Psychophysiological Response to Environmental Tobacco Smoke in an Experimental Social Setting." In: Indoor Air Quality. H. Kasuga (ed.). Berlin, Springer-Verlag, 173-183, 1990.

38. Aronow, W.S., "Effect of Passive Smoking on Angina Pectoris," New England Journal of Medicine 299(1): 21-24, 1978.

39. Hinderliter, A.L., Adams, K.F., Price, C.J., Herbst, M.C., Koch, G. and Sheps, D.S., "Effects of Low-Level Carbon Monoxide Exposure on Resting and Exercise-Induced Ventricular Arrhythmias in Patients with Coronary Artery Disease and No Baseline Ectopy," Archives of Environmental Health 44(2): 89-93, 1989.

40. McNicol, M.W. and Turner, McM., "Oxygen Uptake at the Onset of Angina Pectoris: Effects of Nicotine and Carbon Monoxide," Clinical Science 65(3): 248, 1983.

41. Shephard, R.J., Collins, R. and Silverman, F., "'Passive' Exposure of Asthmatic Subjects to Cigarette Smoke," Environmental Research 20(2): 392-402, 1979.

42. Sheps, D.S., Adams, K.F., Bromberg, P.A., Goldstein, G.M., O'Neil, J.J., Horstman, D. and Koch, G., "Lack of Effect of Low Levels of Carboxyhemoglobin on Cardiovascular Function in Patients with Ischemic Heart Disease," Archives of

2046157572

Source: https://www.industrydocuments.ucsf.edu/docs/qnwl0000

Environmental Health 42(2): 108-116, 1987.

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Source: https://www.industrydocuments.ucsf.edu/docs/qnwl0000

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Response to Question 2a(iii) (continued):

Adult Respiratory Disease and Symptoms

The majority of the studies on spousal smoking and respiratory disease other than cancer in nonsmoking adults have been conducted in the home. Only a few studies have examined the possible relationship between reported exposures to PTS in the workplace and the respiratory health of nonsmoking adults.[1-6] The studies that have been conducted on this issue have reported contradictory results. There are also problems with the methodology utilized in these studies. For example, one often-cited study reported an association between workplace exposure to PTS and small-airways dysfunction in adults,[1] but the authors have been criticized heavily for questionable data acquisition and analysis.[7-15]

Other researchers who have reviewed the reported findings concerning the possible relationship between PTS and respiratory symptoms and diseases in adults also contend that the results are mixed and inconclusive. For example, French researchers, Laurent, et al., have commented that purported long-term health effects from exposure to PTS are difficult to demonstrate in healthy adults and that the results of the epidemiological studies are "sometimes conflicting and often open to question."[16] One investigator has conceded that "the effect of passive smoking on respiratory

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infections in adults has not been well characterized and reports of its effects on chronic respiratory disease in adults have been inconsistent."[17]

In his summary of the studies of respiratory symptoms and disease in adults through early 1990, American investigator Dr. Philip Witorsch noted that "4 of 8 [reported] an increased frequency, 4 of 8 no increased frequency." He stated that, in addition to "all of the problems" with the studies, "these results are too variable to permit any conclusion of association."[18] As his summary demonstrates, the conclusion of the participants at the 1983 U.S. National Institutes of Health workshop on PTS exposure, namely, that the possible effect from PTS "varies from negligible to quite small," is still pertinent.[19]

In addition to inconsistent and variable conclusions, confounding factors are not adequately controlled for in these studies. The same confounders that reportedly affect studies in the home may also play a role in workplace exposure studies. Although some of these confounders, such as gas stove usage, may not directly apply to the indoor air quality of the workplace, exposures in the home to such sources may influence the respiratory health status of the populations studied in the workplace. Potential confounders for adult respiratory health include gas stove usage in the home,[19-20] outdoor air pollution,[21-22]

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socioeconomic status,[23,19] damp housing[19,24-25] and exposure to various indoor air contaminants.[19]

A Discussion of the Published Studies

In 1980, White and Froeb evaluated the possible effect of long-term "passive" smoking and long-term voluntary smoking on specific indexes of pulmonary function in 2,100 middle-aged adults.[1] Eighty-three percent of the subjects held professional, managerial, or technical positions, and the remainder were blue-collar workers. Subjective reports of exposure to active and "passive" smoking were obtained by a self-administered questionnaire.

Nonsmoking subjects indicated on the questionnaire whether smoking was permitted in their working environments. In addition, a portable carbon monoxide analyzer was placed on top of the desk or in the working area of 40 randomly selected nonsmokers who had indicated that they worked in an environment without smoke and 40 similarly selected nonsmokers who had indicated that the air in their working area contained smoke from co-workers. The authors reported that "compared with nonsmokers who worked in environments where there was no smoking, both the men and the women in the other five groups had significantly lower values for FEF 25 to 75 per cent and FEF 75 to 85 per cent." Furthermore, the authors suggested that "the passive smokers not only scored significantly lower than

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their nonsmoking counterparts but also fell into the same state of impaired performance as the noninhalers and light smokers."

The White and Froeb study has been criticized for numerous reasons.[7-10] For example, a physician at a U.S. medical school questioned their use of carbon monoxide as an index of smoke exposure, contending that they "do not have reliable estimates of the smoke exposure in the environment of their nonsmokers" because carbon monoxide is not unique to tobacco smoke.[10] A British reviewer shared the physician's view that their findings "relate to an index which is contentious and certainly not an accepted reliable indicator of an increased health risk."[11] In addition, White and Froeb themselves noted that the average values of the pulmonary tests of nonsmokers exposed to tobacco smoke "were not notably different" from the values suggested as normal by a specialist in this area.[12]

Perhaps the most telling criticisms of the study were voiced by Dr. Michael Lebowitz of the University of Arizona at an annual joint meeting of the American Lung Association/American Thoracic Society and in a subsequent letter published in the U.S. Congressional Record.[13-14] During a forum at the ALA meeting, Dr. Lebowitz stated that he had concluded, from his own extensive review of the study and from an interview with White, that the study was "improperly designed" from an epidemiological point of

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view. He noted that there were problems "inherent" in the study, including the selection of the study group and the measurement of smoke in the workplace. Dr. Lebowitz also expressed concern that the statistical significance of the data appeared to depend on the unexplained omission of data for 3,000 people who were originally included in the study. Based upon these considerations, Dr. Lebowitz urged that the study not be used to support the claim that PTS affects the lung function of adults in the workplace. Dr. Lebowitz again took issue with the White and Froeb study in 1984 in a paper he presented at the Vienna Symposium on Passive Smoking. He contended:

> Even with a biased population, poor study design, and incorrect statistical evaluation, there were no clear-cut, consistent, medically meaningful differences between passive smokers and groups of nonsmokers; a corrected statistical analysis strengthened this conclusion.[15]

In 1984, Kentner, et al., published results of a study assessing the possible influence of reported "passive" smoking on pulmonary function in 1,351 men and women.[2] All subjects were white-collar workers, and the majority were employed in sedentary office jobs. Each subject filled out a self-administered questionnaire, and pulmonary function tests were administered to all of the subjects.

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The authors reported that for one pulmonary function parameter, FVC, the values were similar in all five subgroups of male subjects. Only the current smoking group differed significantly from the three groups of nonsmokers among females. Similar results were reported for $FEF_{25/75}$ and for FEV_1. $FEF_{75/85}$ values reportedly differed significantly in male ex-smokers and current smokers as compared with non-smokers and men reportedly exposed to PTS. For $MEF_{25/75}$, male ex-smokers differed from both male "passive" and current smokers, while female non-smokers and ex-smokers differed from current smokers. Reported "passive" smokers showed essentially no decrease in lung function parameters. The authors concluded that "it seems that the passive inhalation of tobacco smoke at home or in the workplace by healthy individuals probably does not lead to any essential impairment of pulmonary function." The authors also reported these findings in 1988 and 1990 publications.[3-4]

In 1989, Kentner, et al., reported on their investigations of pulmonary function in adults reportedly exposed to "passive" smoking in the workplace.[5] In the years 1983-1984, they examined 1,364 employees with healthy lungs from three different companies. Information concerning tobacco smoke exposure was taken from a standardized questionnaire.

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Bronchopulmonary function was checked with the flow-volume curve. The authors again reported that "everyday passive exposure to smoke in the office or at home does not cause a significant impairment of lung function in adults with healthy lungs." The authors also raised the question as to the extent to which the reported "passive" smoking-induced impairment by White and Froeb and others "is at all relevant pathophysiologically." They wrote that "it may be assumed that, under normal, everyday conditions, exposure of adults with healthy lungs to passive smoke does not lead to relevant pathological changes in the bronchopulmonary function in the sense of adverse effects."

In a 1991 study, White, Froeb and Kulik monitored CO levels (as an index of cigarette smoke in the workplace) and analyzed diary entries on respiratory symptoms, eye irritation, chest colds, and lost days from work due to respiratory illness in 40 nonsmokers reportedly chronically exposed to PTS in the workplace.[6]

Exposure to environmental pollution, smoking and physical characteristics were assessed from a self-administered questionnaire completed during the course of the study. The self-reported PTS exposed subjects met the same characteristics as the nonexposed nonsmokers, only they had reported exposures to PTS in the workplace for at least one year. To obtain "objective measures

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of tobacco smoke concentrations," a single trained technician visited the work site on three occasions. The CO levels were recorded continuously for 24 hours. Results from the three days were then averaged.

Each subject responded to a questionnaire developed by the American Thoracic Society during one of the three visits. The questionnaire solicited information on respiratory symptoms including chronic cough, chronic phlegm, breathlessness, chest colds and chest illnesses, number of days missed from work due to chest cold or chest illness, and eye irritation.

The authors concluded that "chronic exposure to tobacco smoke in the work place produces significant eye irritation and increases respiratory symptoms and the incidence of chest colds." However, the authors failed to control for various confounding factors that might have affected this reported association. For example, dietary factors, gas cooking at home, and bioaerosols in the workplace were not controlled for in this study. Furthermore, carbon monoxide is not an accurate assessment of exposure to PTS because tobacco smoke is not the only potential source of CO in the indoor environment.[10] Therefore, the authors' conclusion that PTS in the workplace has deleterious effects on the respiratory health of adults is not justified by the scientific data.

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Conclusion

The studies on workplace exposure to PTS and the respiratory health of nonsmoking adults are inconsistent in their reported results. Furthermore, the single study which reports an association between workplace exposure to PTS and small airways dysfunction in adults has been heavily criticized for questionable data acquisition and analysis. Thus, the data do not support the conclusion that PTS exposure in the workplace contributes to chronic respiratory disease and symptoms in nonsmoking adults.

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REFERENCES

1. White, J.R. and Froeb, H.F., "Small-Airways Dysfunction in Nonsmokers Chronically Exposed to Tobacco Smoke," The New England Journal of Medicine 302 (13): 720-723, 1980.

2. Kentner, M., Triebig, G. and Weltle, D., "The Influence of Passive Smoking on Pulmonary Function - A Study of 1,351 Office Workers, Preventive Medicine 13(6): 656-669, 1984.

3. Kentner, M. and Weltle, D., "Passive Tobacco Smoke Inhalation and Lung Function in Adults." In: Indoor and Ambient Air Quality. R. Perry and P. Kirk (eds.). London, Selper Ltd., 232-241, 1988.

4. Kentner, M. and Weltle, D., "Are There Any Impairments of Maximal Expiratory Flow-Volume Curves by Passive Smoking?" In: Indoor Air Quality. H. Kasuga (ed.). Berlin, Heidelberg, Springer-Verlag, 153-166, 1990.

5. Kentner, M., Weltle, D. and Valentin, H., "Passive Smoking and Lung Function in Adults," Arbeitsmedicine Sozialmedicine Praventivmedicine (24): 8-13, 1989.

6. White, J.R., Froeb, H.F. and Kulik, J.A., "Respiratory Illness in Nonsmokers Chronically Exposed to Tobacco Smoke in the Work Place," Chest 100(1): 39-43, 1991.

7. Adlkofer, F., Scherer, G. and Weimann, H., "Small-Airways Dysfunction in Passive Smokers," New England Journal of Medicine 303(7): 392, 1980.

8. Huber, G., "Small-Airways Dysfunction in Passive Smokers," New England Journal of Medicine 303(7): 392, 1980.

9. Freedman, A., "Small-Airways Dysfunction in Passive Smokers," New England Journal of Medicine 303(7): 393, 1980.

10. Aviado, D., "Small-Airways Dysfunction in Passive Smokers," New England Journal of Medicine 303(7): 393, 1980.

11. Lee, P.N., "Passive Smoking," Food Chemistry and Toxicology 20: 223-229, 1982.

12. White, J. and Froeb, H., "Small-Airways Dysfunction in Passive Smokers," New England Journal of Medicine 303(7): 393-394, 1980.

2046157584

Source: https://www.industrydocuments.ucsf.edu/docs/qnwl0000

13. Lebowitz, M., "Forum: Second Hand Smoke -- How Dangerous?," Presentation to the American Lung Association/American Thoracic Society Annual Meeting, Los Angeles, California, May 17, 1982.

14. Fountain, L.H., Statement Re: "White-Froeb Study Discredited by Scientists." In: U.S. Congressional Record, 97th Congress, 2nd Session, E5252-5254, December 16, 1982.

15. Lebowitz, M., "Influence of Passive Smoking on Pulmonary Function: A Survey," Preventive Medicine 13(6): 645-655, 1984.

16. Laurent, A.M., Courtois, Y.A., Pretet, S. and Claude, J.R., "Evaluation of Exposure to Ambient Tobacco Smoke: A Few Concrete Examples Concerning the Value of Biological Atmospheric Indicators." In: Present and Future of Indoor Air Quality. C.J. Bieva, Y. Courtois, M. Govaerts (eds.). Amsterdam, Excerpta Medica, 103-110, 1989.

17. Graham, N.M.H., "The Epidemiology of Acute Respiratory Infections in Children and Adults: A Global Perspective," Epidemiologic Reviews 12: 149-178, 1990.

18. Witorsch, P., "Health Effects of Environmental Tobacco Smoke." In: Toxicology Forum: 1990 Annual Winter Meeting. Washington D.C., 212, February 19-21, 1990.

19. U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health, Report of Workshop on Respiratory Effects of Involuntary Smoke Exposure: Epidemiologic Studies, May 1-3, 1983, December, 1983.

20. Koo, L.C. and Ho, J.H.C., "Sources of Nitrogen Dioxide in Homes and Its Association with Respiratory Illness in Hong Kong." In: Indoor Air Quality and Ventilation. London, Selper Ltd., 287-294, 1990.

21. Detels, R., Tashkin, D.P., Sayre, J.W., Rokaw, S.N., Massey, F.J., Coulson, A.H. and Wegman, D.H., "The UCLA Population Studies of CORD: X. A Cohort Study of Changes in Respiratory Function Associated with Chronic Exposure to SOx, NOx, and Hydrocarbons," American Journal of Public Health 81(3): 350-359, 1991.

22. Xu, X., Dockery, D.W. and Wang, L., "Effects of Air Pollution on Adult Pulmonary Function," Archives of Environmental Health 46(4): 198-206, 1991.

2046157585

Source: https://www.industrydocuments.ucsf.edu/docs/qnwl0000

23. Holma, B. and Winding, O., "Housing, Hygiene, and Health: A Study in Old Residential Areas in Copenhagen," Archives of Environmental Health (March/April): 86-93, 1977.

24. Platt, S.D., Martin, C.J., Hunt, S.M. and Lewis, C.W., "Damp Housing, Mould Growth, and Symptomatic Health State," British Medical Journal 298: 1673-1678, 1989.

25. Dales, R.E., Burnett, R. and Zwanenburg, H., "Adverse Health Effects Among Adults Exposed to Home Dampness and Molds," American Review of Respiratory Disease 143(3): 505-509, 1991.

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Response to Question 2a(iii) (continued):

Parental Smoking

While parental smoking studies are not directly related to workplace indoor air quality issues, they comprise a large proportion of the available studies on PTS, and are often cited by those who argue that PTS exposures are associated with respiratory disease and symptoms in nonsmokers. However, the scientific basis for the claim that PTS is associated with respiratory diseases and symptoms in children is difficult to interpret.

A Discussion of the Published Studies

While one study on parental smoking examines respiratory symptoms or illness such as coughs and colds by questionnaire responses from parents,[1] another measures lung function with special equipment at a school or health facility.[2] In the U.S. alone, according to one report, this has led to a situation in which studies of PTS and the respiratory system are "being carried out by at least three different groups, are employing different populations and methodologies and have led to varying conclusions.[3]

Perhaps not surprisingly, studies of parental smoking, each with a different sample size, data collection method, and analysis, tend to yield factually incompatible and contrary

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conclusions. For instance, although certain studies have reported adverse findings between parental smoking and respiratory illness in children,[4-35] others have observed no significant relationship.[1,36-51] After a five-year study of over 400 children, for example, a Dutch research group concluded there was "no evidence" that parental smoking had an appreciable effect on respiratory symptoms in school children.[43] A similar conclusion was reached by a group of U.S. researchers, including a critic of smoking, who found "no significant relation" between parental smoking and respiratory symptoms in a study of nearly 400 families with 816 children in three cities.[36]

The contradictory nature of findings on the issue of parental smoking is also apparent in the growing number of studies examining the relationship between parental smoking and children's respiratory or lung function. Although several reports have claimed that parental smoking results in decreased pulmonary function in children,[8,13-14,32,52-60] others have not,[61-64] including those of a U.S. research group who have published a series of studies on this subject.[2,65-67] In 1982, for example, the U.S. group showed that a comparison of body size with lung function eliminated any reported correlation between parental smoking and children's lung function.[2] Two years later, a reanalysis of data from families in their study population again showed that "parental smoking did not have a significant effect on children's pulmonary function; smoking habits

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of others in the household (predominantly siblings) did not have any effect either."[66]

Confounding Factors and Other Sources of Bias

The authors of studies reporting adverse effects from PTS exposures among children concede that their conclusions must be viewed with caution because of numerous confounding factors. The potential impact of such factors was given special consideration in the report from a workshop on PTS sponsored by the U.S. National Institutes of Health.[3] After listing numerous such factors, including types of heating used, socio-economic status and demographic and medical characteristics of the study population, the report cautioned "that any study which ignores them will be seriously flawed."

The importance of such factors in evaluating the outcome of research on parental smoking is supported by a number of reports which have shown that the use of gas stoves in the home may be independently associated with respiratory disease[40,65,68-72] and impaired pulmonary performance[73-74] in children. One group of British researchers acknowledged the possible influence of factors such as cross-infection in the home and genetic susceptibility to childhood respiratory illness and symptoms.[11-12] More recently, researchers in Hong Kong reported "a highly significant correlation"

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between the frequency of respiratory illnesses of mothers and their children.[75]

Other confounding factors independent of parental smoking have been reported recently in the literature. For example, studies in the United Kingdom have identified damp housing[46,76-79] and paternal occupation[80] as potential explanatory factors for the occurrence of respiratory illness in children. Other recent studies have identified outdoor air pollution,[82-85] infections transmitted during day-care attendance,[49,86-87] decreased breast-feeding[88] and the use of kerosene heaters and woodburning stoves in the home[89-91] as factors related to childhood respiratory disease.

The relevance of dampness in the etiology of respiratory symptoms in children is supported by current research which links dampness with the presence of molds, dust mites, fungi and other allergenic microbes. The growth of fungi and molds in the home is directly related to respiratory symptoms and sensitization reactions in some individuals.[78,92-94] Recent investigations report, moreover, that exposure to PTS does not increase sensitization to common allergens in children.[95-96]

Others have conceded that the reliance of such studies on questionnaires for information about respiratory symptoms casts doubt on their reported findings. In one study that reported a

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significant association between parental smoking and respiratory symptoms, for example, it was noted that even "slight changes" in the way the questions were phrased could result "in substantial differences in the type of responses one obtains."[14] Similarly, another study observed that there was a significant difference in the respiratory symptoms reported depending on which parent completed the questionnaire.[24] Authors of another study that reported adverse effects of parental smoking on the respiratory health of children conceded that "since the exposure variables used in these analyses were subject to substantial measurement error, a more refined measurement of personal exposure is required."[29] One researcher who is critical of parental smoking has stated that "quantitative assessment of involuntary exposure of infants and children to ETS has been very imprecise and probably inaccurate."[97]

Studies utilizing seemingly more objective standards such as actual measurements of lung function are also open to criticism. Even reviewers of the literature who are critical of parental smoking concede that the tests used in these studies are "influenced by a large number of variables."[98] They list age, height, and gender of the test subject as well as his or her motivation, cooperation, and effort put forth during the test, the skill and experience of the operator, and the type of instrumentation used as variables that can affect the results of

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pulmonary function measurements. The reviewers explain that these problems are especially important in pulmonary function measures taken in children. In 1989, two American co-researchers, Witorsch and Witorsch, reported that "it has been shown that mean pulmonary performance within a single group of children can vary significantly from one spirometry test to the next without any apparent cause" and that it "is noteworthy that such statistically significant differences are similar in magnitude to most of the small decrements in pulmonary function reported in children of smoking parents."[99]

The shortcomings of studies analyzing the relationship between PTS exposure and childhood health were highlighted in a 1988 report by two U.S. investigators who re-examined 30 such studies and evaluated them for their scientific validity.[100] They noted that while several studies of adequate scientific design have reported a statistically significant relationship between PTS exposures and childhood health, "most studies had significant design problems that prevent reliance on their conclusions." The authors concluded that "many questions remain, and future studies should consider important methodological standards to determine more accurately the effect of passive smoking on child health."

Thus, claims that parental smoking plays a causal role in the development of respiratory symptoms and reduced lung function in children are not scientifically justified. Such claims are

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typically based upon a single study of a selected symptom (such as cough or wheeze). These kinds of studies invariably fail to consider nutrition, health habits of the family, and other lifestyle variables. Similarly, studies that report reduced lung function in children of smoking parents fail to address the issue of socio-economic status or the potential role of genetic and family traits in pulmonary function capabilities.[64] Moreover, the reductions reported in the literature are small and of uncertain clinical or biological significance, and are contradicted by a number of studies that reportedly have observed no effect of parental smoking on children's lung function.

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REFERENCES

1. Camacho, E., Colomer, P.R. and Betoret, J.L.D., "Pulmonary Symptoms and Pulmonary Functional Tests Among Children in Relation to the Area of Residence," European Respiratory Diseases 63(2): 165-166, 1982.

2. Lebowitz, M., Armet, D.B. and Knudson, R., "The Effect of Passive Smoking on Pulmonary Function in Children," Environment International 8: 371-373, 1982.

3. U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health, Report of Workshop on Respiratory Effects of Involuntary Smoke Exposure: Epidemiologic Studies, May 1-3, 1983, December, 1983.

4. Committee on Passive Smoking, Board on Environmental Studies and Toxicology, National Research Council, Environmental Tobacco Smoke: Measuring Exposures and Assessing Health Effects. Washington, D.C., National Academy Press, 1986.

5. U.S. Department of Health and Human Services, Public Health Services, Office on Smoking and Health, The Health Consequences of Involuntary Smoking: A Report of the Surgeon General. DHHS Publication No. (CDC) 87-8398, Washington, D.C., U.S. Government Printing Office, 1986.

6. Bland, M., Bewley, B.R., Pollard, V. and Banks, M.H., "Effect of Children's and Parents' Smoking on Respiratory Symptoms," Archives of Diseases in Childhood 53(2): 100-105, 1978.

7. Bonham, G. and Wilson, R., "Children's Health in Families With Cigarette Smokers," American Journal of Public Health 71(3): 290-293, 1981.

8. Burchfiel, C., Higgins, M.W., Keller, J.B., Howatt, W.F., Butler, W.J. and Higgins, I.T.T., "Passive Smoking in Childhood: Respiratory Conditions and Pulmonary Function in Tecumseh, Michigan," American Review of Respiratory Disease 133(6): 966-973, 1986.

9. Cameron, P. and Robertson, D., "Effect of Home Environment Tobacco Smoke on Family Health," Journal of Applied Psychology 57(2): 142-147, 1973.

10. Chen, Y., "Synergistic Effect of Passive Smoking and Artificial Feeding on Hospitalization for Respiratory Illness in Early Childhood," Chest 95: 1004-1007, 1989.

2046157595

Source: https://www.industrydocuments.ucsf.edu/docs/qnwl0000

11. Colley, J., "Respiratory Symptoms in Children and Parental Smoking and Phlegm Production," British Medical Journal II: 201-204, 1974.

12. Colley, J., Holland, W.W. and Corkhill, R.T., "Influence of Passive Smoking and Parental Phlegm on Pneumonia and Bronchitis in Early Childhood," Lancet II: 1031-1034, 1974.

13. Dockery, D., Speizer, F.E., Stram, D.O., Ware, J.H., Spengler, J.D. and Ferris, B.G., "Effects of Inhalable Particles on Respiratory Health of Children," American Review of Respiratory Disease 139: 587-594, 1989.

14. Ekwo, E., Weinberger, M.M., Lachenbruch, P.A. and Huntley, W.H., "Relationship of Parental Smoking and Gas Cooking to Respiratory Disease in Children," Chest 84(6): 662-668, 1983.

15. Fergusson, D., Horwood, L.J., Shannon, F.T. and Taylor, B., "Parental Smoking and Lower Respiratory Illness in the First Three Years of Life," Journal of Epidemiology and Community Health 35(3): 180-184, 1981.

16. Fergusson, D. and Horwood, L.J., "Parental Smoking and Respiratory Illness During Early Childhood: A Six-year Longitudinal Study," Pediatric Pulmonology 1(2): 99-106, 1985.

17. Ferris, B., Dockery, D.W., Ware, J.H., Speizer, F.E. and Spiro, R., "The Six-City Study: Examples of Problems in Analysis of Data," Environmental Health Perspectives 52: 115-123, 1983.

18. Gortmaker, S., Walker, D.K., Jacobs, F.H. and Ruch-Ross, H., "Parental Smoking and the Risk of Childhood Asthma," American Journal of Public Health 72(6): 574-579, 1982.

19. Harlap, S. and Davies, A., "Infant Admissions to Hospital and Maternal Smoking," Lancet I: 529-532, 1974.

20. Kraemer, M., Richardson, M.A., Weiss, N.S., Furukawa, C.T., Shapiro, G.G., Pierson, W.E. and Bierman, C.W., "Risk Factors for Persistent Middle Ear Effusions: Otitis Media, Catarrh, Cigarette Smoke Exposure, and Atopy," Journal of the American Medical Association 249(8): 1022-1025, 1983.

21. Murray, A. and Morrison, B., "Passive Smoking and the Seasonal Difference of Severity of Asthma in Children," Chest 94(4): 701-708, 1988.

2046157596

Source: https://www.industrydocuments.ucsf.edu/docs/qnwl0000

22. Neuspiel, D., Rush, D., Butler, N.R., Golding, J., Bijur, P.E. and Kurzon, M., "Parental Smoking and Post-Infancy Wheezing in Children: A Prospective Cohort Study," American Journal of Public Health 79(2): 168-171, 1989.

23. Ogston, S., Florey, C.D.V. and Walker, C.H.M., "Association of Infant Alimentary and Respiratory Illness with Parental Smoking and Other Environmental Factors," Journal of Epidemiology and Community Health 41(1): 21-25, 1987.

24. Schenker, M., Samet, J.M. and Speizer, F.E., "Risk Factors for Childhood Respiratory Disease: The Effect of Host Factors and Home Environmental Exposures," American Review of Respiratory Disease 128: 1038-1043, 1983.

25. Somerville, S., Rona, R.J. and Chinn, S., "Passive Smoking and Respiratory Conditions in Primary School Children," Journal of Epidemiology and Community Health 42(2): 105-110, 1988.

26. Strachan, D., Jarvis, M.J. and Feyerabend, C., "Passive Smoking, Salivary Cotinine Concentrations, and Middle Ear Effusion in 7 Year Old Children," British Medical Journal 298: 1549-1552, 1989.

27. Tsimoyianis, G., Jacobson, M.S., Feldman, J.G., Antonio-Santiago, M.T., Clutario, B.C., Nussbaum, M. and Schenker, I.R., "Reduction in Pulmonary Function and Increased Frequency of Cough Associated With Passive Smoking in Teenage Athletes," Pediatrics 80(1): 32-36, 1987.

28. Ware, J., Dockery, D.W., Spiro, A., Speizer, F.E. and Ferris, B.G., "Passive Smoking, Gas Cooking, and Respiratory Health of Children Living in Six Cities," American Review of Respiratory Disease 129: 366-374, 1984.

29. Ugnat, A.M., Mao, Y., Miller, A.B. and Wigle, D.T., "Effects of Residential Exposure to Environmental Tobacco Smoke on Canadian Children," Canadian Journal of Public Health 81(5): 345-349, 1990.

30. Greenberg, R.A., Bauman, K.E., Glover, L.H., Strecher, V.J., Kleinbaum, D.G., Haley, N.J., Stedman, H.C., Fowler, M.G. and Loda, F.A., "Ecology of Passive Smoking by Young Infants," Journal of Pediatrics 114: 774-780, 1989.

31. Berg, A.T., Shapiro, E.D. and Capobianco, L.A., "Group Day Care and the Risk of Serious Infectious Illnesses," American Journal of Epidemiology 133(2): 154-163, 1991.

2046157597

Source: https://www.industrydocuments.ucsf.edu/docs/qnwl0000

32. Dijkstra, L., Houthuijs, D., Brunekreef, B., Akkerman, I. and Boleij, J.S.M., "Respiratory Health Effects of the Indoor Environment in a Population of Dutch Children," American Review of Respiratory Disease 142: 1172-1178, 1990.

33. McConnochie, K.M. and Roghmann, K.J., "Wheezing at 8 and 13 Years: Changing Importance of Bronchiolitis and Passive Smoking," Pediatric Pulmonology 6(3): 138-146, 1989.

34. Woodward, A., Douglas, R.M., Graham, N.M. and Miles, H., "Acute Respiratory Illness in Adelaide Children: Breast Feeding Modifies the Effect of Passive Smoking," Journal of Epidemiology and Community Health 44: 224-230, 1990.

35. Stern, B., Raizenne, M. and Burnett, R., "Respiratory Effects of Early Childhood Exposure To Passive Smoke," Environment International 15: 29-34, 1989.

36. Schilling, R., Letai, A.D., Hui, S.L., Beck, G.J., Schoenberg, J.B. and Bouhuys, A., "Lung Function, Respiratory Disease, and Smoking in Families," American Journal of Epidemiology 106(4): 274-283, 1977.

37. Binder, R., Mitchell, C.A., Hosein, H.R. and Bouhuys, A., "Importance of the Indoor Environment in Air Pollution Exposure," Archives of Environmental Health 31(6): 277-279, 1976.

38. Bouhuys, A., Lung Diseases in Rural and Urban Communities, Report Number HR-42912-1F, Sponsored by the Division of Lung Diseases, National Heart, Lung and Blood Institute, U.S. National Institutes of Health, Bethesda, Maryland, 77-89, June 10, 1977.

39. Gardner, G., Frank, A.L. and Taber, L.H., "Effects of Social and Family Factors on Viral Respiratory Infection and Illness in the First Year of Life," Journal of Epidemiology and Community Health 38: 42-48, 1984.

40. Harrington, W. and Krupnick, A., "Short-Term Nitrogen Dioxide Exposure and Acute Respiratory Disease in Children," Journal of the Air Pollution Control Association 35: 1061-1067, 1985.

41. Holma, B. and Winding, O., "Housing, Hygiene, and Health: A Study in Old Residential Areas in Copenhagen," Archives of Environmental Health 32(2): 86-93, 1977.

42. Kallail, K., Rainbolt, H.R. and Bruntzel, M.D., "Passive Smoking and Middle Ear Problems in Kansas Public School

2046157598

Source: https://www.industrydocuments.ucsf.edu/docs/qnwl0000

Children," Journal of Communicable Disorders 20: 187-196, 1987.

43. Kerrebijn, J., Hoogeveen-Schroot, H.C.A. and van der Wal, M.C., "Chronic Nonspecific Respiratory Disease in Children, A Five Year Follow-Up Study," Acta Paediatr Scand Suppl. 261: 11-72, 1977.

44. Lebowitz, M. and Burrows, B., "Respiratory Symptoms Related to Smoking Habits of Family Adults," Chest 69(1): 48-50, 1976.

45. Love, G., Lan, S.P., Shy, C.M. and Struba, R.J., "The Incidence and Severity of Acute Respiratory Illness in Families Exposed to Different Levels of Air Pollution, New York Metropolitan Area, 1971-72," Archives of Environmental Health 36(2): 66-73, 1981.

46. Martin, C., Platt, S.D. and Hunt, S.M., "Housing Conditions and Ill Health," British Medical Journal 294: 1125-1127, 1987.

47. Salzman, M., Biller, H.F. and Schechter, C.B., "Passive Smoking and Croup," Archives of Otolaryngology and Head Neck Surgery 113: 866-868, 1987.

48. Shy, C., Creason, J.P., Pearlman, M.E., McClain, K.E., Benson, F.B. and Young, M.M., "The Chattanooga School Children Study: Effects of Community Exposure to Nitrogen Dioxide. II. Incidence of Acute Respiratory Illness," Journal of the Air Pollution Control Association 20(9): 582-588, 1970.

49. Harsten, G., Prellner, K., Heldrup, J., Kalm, O. and Kornfalt, R., "Acute Respiratory Tract Infections in Children: A Three-Year Follow-up from Birth," Acta Paediatr Scand 79(4): 402-409, 1990.

50. Thorton, A.J., Morley, C.J., Hewson, P.H., Cole, T.J., Fowler, M.A. and Tunnacliffe, J.M., "Symptoms in 298 Infants Under 6 Months Old, Seen at Home," Archives of Disease in Childhood 65(3): 280-285, 1990.

51. Victora, C.G., Smith, P.G., Barros, F.C., Vaughan, J.P. and Fuchs, S.C., "Risk Factors for Deaths Due to Respiratory Infections Among Brazilian Infants," International Journal of Epidemiology 18(4): 918-925, 1989.

52. Berkey, C., Ware, J.H., Dockery, D.W., Ferris, B.G. and Speizer, F.E., "Indoor Air Pollution and Pulmonary Function Growth in Preadolescent Children," American Journal of Epidemiology 123(2): 250-260, 1986.

2046157599

Source: https://www.industrydocuments.ucsf.edu/docs/qnwl0000

53. Chen, Y. and Li, W., "The Effect of Passive Smoking on Children's Pulmonary Function in Shanghai," American Journal of Public Health 76(5): 515-518, 1986.

54. Corbo, G., Foresi, A., Valente, S. and Bustacchini, S., "Maternal Smoking and Bronchial Responsiveness in Children," American Review of Respiratory Disease 137(1): 245, 1987.

55. Hasselblad, V., Humble, C.G., Graham, M.G. and Anderson, H.S., "Indoor Environmental Determinants of Lung Function in Children," American Review of Respiratory Disease 123(5): 479-485, 1981.

56. Kauffmann, F., Tager, I.B., Munoz, A. and Speizer, F.E., "Familial Factors Related to Lung Function in Children Aged 6-10 Years," American Journal of Epidemiology 129(6): 1289-1299, 1989.

57. Masi, M., Hanley, J.A., Ernst, P. and Becklake, M.R., "Environmental Exposure to Tobacco Smoke and Lung Function in Young Adults," American Review of Respiratory Disease 138: 296-299, 1988.

58. Tager, I., Munoz, A., Rosner, B., Weiss, S.T., Carey, V. and Speizer, F.E., "Effect of Cigarette Smoking on the Pulmonary Function of Children and Adolescents," American Review of Respiratory Disease 131(5): 752-759, 1985.

59. Tager, I., Weiss, S.T., Munoz, A., Rosner, B. and Speizer, F.E., "Longitudinal Study of the Effects of Maternal Smoking on Pulmonary Function in Children," New England Journal of Medicine 309(120): 699-703, 1983.

60. Tashkin, D., Clark, V.A., Simmons, M., Reems, C., Coulson, A.H., Bourque, L.B., Sayre, J.W., Detels, R. and Rokaw, S., "The UCLA Population Studies of Chronic Obstructive Respiratory Disease. VII. Relationship Between Parental Smoking and Children's Lung Function," American Review of Respiratory Disease 129: 891-897, 1984.

61. Dodge, R., "The Effects of Indoor Pollution on Arizona Children," Archives of Environmental Health 37(3): 151-155, 1982.

62. Hosein, R. and Corey, P., "Multivariate Analysis of Nine Indoor Factors on FEV_1 of Caucasian Children," American Thoracic Society Meeting, Miami Beach, Florida, May 20-23, 1984. Poster Session #32.

2046157600

Source: https://www.industrydocuments.ucsf.edu/docs/qnwl0000

63. Mandi, A., Galambos, E., Galgoczy, G., Szabo, M. and Kollar, K., "Relationship Between Lung Function Values and Air Pollution Data in Budapest School Children," Pneumonologie 150(2/4): 217-225, 1974.

64. Witorsch, R. and Witorsch, P., "Maternal Smoking and Pulmonary Performance in Children: A Critical Analysis," Indoor Air '87, Proceedings of the 4th International Conference on Indoor Air Quality and Climate, Berlin, 175-179, August 17-21, 1987.

65. Lebowitz, M., "The Effects of Environmental Tobacco Smoke Exposure and Gas Stoves on Daily Peak Flow Rates in Asthmatic and Non-Asthmatic Families." In: ETS-Environmental Tobacco Smoke: Report from a Workshop on Effects and Exposure Levels. R. Rylander, Y. Peterson and M.-C. Snella (eds.). Published simultaneously in European Journal of Respiratory Diseases, Supplement No. 133, Vol. 65, 90-97, 1984.

66. Lebowitz, M., Knudson, R.J. and Burrows, B., "Family Aggregation of Pulmonary Function Measurements," American Review of Respiratory Disease 129: 8-11, 1984.

67. Lebowitz, M., Holberg, C.J., Boyer, B. and Hayes, C., "Respiratory Symptoms and Peak Flow Associated with Indoor and Outdoor Air Pollutants in the Southwest," Journal of the Air Pollution Control Association 35: 1154-1158, 1985.

68. Melia, R., Florey, C.D.V., Altman, D.G. and Swan, A.V., "Association Between Gas Cooking and Respiratory Disease in Children," British Medical Journal II: 149-152, 1977.

69. Melia, R., Florey, C.D.V., Morris, R.W., Goldstein, B.D., John, H.H., Clark, D., Craighead, I.B. and Mackinlay, J.C., "Childhood Respiratory Illness and the Home Environment II. Association Between Respiratory Illness and Nitrogen Dioxide, Temperature and Relative Humidity," International Journal of Epidemiology 11(2): 164-169, 1982.

70. Melia, R., Chinn, S. and Rona, R.J., "Respiratory Illness and Home Environment of Ethnic Groups," British Medical Journal 296: 1438-1441, 1988.

71. Melia, R., Florey, C.D.V. and Chinn, S., "The Relation Between Respiratory Illness in Primary School Children and the Use of Gas for Cooking. I -- Results from a National Survey," International Journal of Epidemiology 8(4): 333-338, 1979.

72. Speizer, F., Ferris, B., Bishop, Y.M.M. and Spengler, J., "Respiratory Disease Rates and Pulmonary Function in Children

2046157601

Source: https://www.industrydocuments.ucsf.edu/docs/qnwl0000

Associated with NO_2 Exposure," American Review of Respiratory Disease 121: 3-10, 1980.

73. Jedrychowski, W., Khogali, M. and Karim, M.A., "Height and Lung Function in Preadolescent Children of Kuwaitis and European Origin. The Pilot Survey on Health Effect of Gas Cooking in the Middle-East." In: Indoor Air Quality and Ventilation. London, Selper Ltd., Volume 2, 175-181, 1990.

74. Brunekreef, B., Houthuijs, D., Dijkstra, L. and Soleij, J.S.M., "Indoor Nitrogen Dioxide Exposure and Children's Pulmonary Function," Journal of the Air and Waste Management Association 40(9): 1252-1256, 1990.

75. Koo, L.C., Ho, J.H.C., Matsuki, H., Shimizu, H., Mori, T. and Tominaga, S., "A Comparison of the Prevalence of Respiratory Illnesses Among Nonsmoking Mothers and Their Children in Japan and Hong Kong," American Review of Respiratory Disease 138: 290-295, 1988.

76. Strachan, D. and Elton, R., "Relationship Between Respiratory Morbidity in Children and the Home Environment," Family Practice 3(3): 137-142, 1986.

77. Strachan, D., "Damp Housing and Childhood Asthma: Validation of Reporting of Symptoms," British Medical Journal 297: 1223-1226, 1988.

78. Platt, S.D., Martin, C.J., Hunt, S.M. and Lewis, C.W., "Damp Housing, Mould Growth, and Symptomatic Health State," British Medical Journal 298: 1673-1678, 1989.

79. Brunekreef, B., Dockery, D., Speizer, F.E., Ware, J.H., Spengler, J.D. and Ferris, B.G., "Home Dampness and Respiratory Morbidity in Children," American Review of Respiratory Disease 140: 1363-1367, 1989.

80. Watkins, C., Sittampalam, Y., Morrell, D.C., Leeder, S.R. and Tritton, E., "Patterns of Respiratory Illness in the First Year of Life," British Medical Journal 293: 794-796, 1986.

81. Kerigan, A., Goldsmith, C.H. and Pengelly, L.D., "A Three-Year Cohort Study of the Role of Environmental Factors in the Respiratory Health of Children in Hamilton, Ontario: Epidemiologic Survey, Design, Methods, and Description of Cohort," American Review of Respiratory Disease 133: 987-993, 1986.

2046157602

Source: https://www.industrydocuments.ucsf.edu/docs/qnwl0000

82. Goren, A. and Hellmann, S., "Prevalence of Respiratory Symptoms and Diseases in Schoolchildren Living in a Polluted and in a Low Polluted Area in Israel," Environmental Research 45(1): 28-37, 1988.

83. Pope, C., "Respiratory Disease Associated with Community Air Pollution and a Steel Mill, Utah Valley," American Journal of Public Health 79(5): 623-628, 1989.

84. Frischer, T., Studnicka, M., Hesse, P. and Neumann, M., "Effects of Traffic Emissions on the Airways in Children," Pneumologie 44: 890-891, 1990.

85. Rutishauser, M., Ackermann, U., Braun, C., Gnehm, H.P. and Wanner, H.U., "Significant Association between Outdoor NO_2 and Respiratory Symptoms in Preschool Children," Lung, Supplement 168: 347-352, 1990.

86. Fleming, D., Cochi, S.L., Hightower, A.W. and Broome, C.V., "Childhood Upper Respiratory Tract Infections: To What Degree is Incidence Affected by Day Care Attendance?," Pediatrics 79(1): 55-60, 1987.

87. Hurwitz, E.S., Gunn, W.J., Pinsky, P.F. and Schonberger, L.B., "Risk of Respiratory Illness Associated with Day-Care Attendance: A Nationwide Study," Pediatrics 87(1): 62-69, 1991.

88. Wright, A.L., Holberg, C.J., Martinez, F.D., Morgan, W.J. and Taussig, L.M., "Breast Feeding and Lower Respiratory Tract Illness in the First Year of Life," British Medical Journal 299: 946-949, 1989.

89. Berwick, M., Zagraniski, R.T., Leaderer, B.P. and Stolwijk, J.A., "Respiratory Illness in Children Exposed to Unvented Combustion Sources." In: Indoor Air. Volume 2: Radon, Passive Smoking, Particulates and Housing Epidemiology. B. Berglund, T. Lindvall and J. Sundell (eds.). Stockholm, Swedish Council for Building Research, 255-260, 1984.

90. Osborne, J. and Honicky, R., "Health Effects of Heating With Wood: Chest Illness in Young Children and Indoor Heating with Woodburning Stoves." In: IAQ '89. The Human Equation: Health and Comfort. American Society of Heating, Refrigeration and Air-Conditioning Engineers, and the Society for Occcupational and Environmental Health, San Diego, California, April 17-20, 1989. Abstract.

2046157603

Source: https://www.industrydocuments.ucsf.edu/docs/qnwl0000

91. Morris, K., Morganlander, M., Coulehan, J.L., Gahagen, S. and Arena, V.C., "Wood-Burning Stoves and Lower Respiratory Tract Infection in American Indian Children," American Journal of Diseases in Childhood 144: 105-108, 1990.

92. Nordvall, S., Eriksson, M., Rylander, E. and Schwartz, B., "Sensitization of Children in the Stockholm Area to House Dust Mites," Acta Paediatr Scand 77: 716-720, 1988.

93. Rylander,R., Sorensen, S., Goto,- H., Yuasa, K. and Tanaka, S., "The Importance of Endotoxin and Glucan for Symptoms in Sick Buildings." In: Indoor Air Quality: Symposium. Buenos Aires, National Academy of Sciences of Buenos Aires, 157-164, 1989.

94. Kort, H., van Bronswijk, J. and Schober, G., "Moulds, Mites and Moisture: A Preliminary Report on Six Cases of Fungal Damage in Dwellings." In: Present and Future of Indoor Air Quality. C. Bieva, Y. Courtois, M. Govaerts (eds.). Amsterdam, Excerpta Medica, 389-394, 1989.

95. Ownby, D. and McCullough, J., "Passive Exposure to Cigarette Smoke Does Not Increase Allergic Sensitization in Children," Journal of Allergy and Clinical Immunology 82(4): 634-638, 1988.

96. Johnson, C., Ownby, D., Stauchman, C., Blocki, S., Birg, G., Jacobsen, G. and McCullough, J., "Determinants of Immunoglobulin E (IgE) at Birth," American Journal of Epidemiology 132(4): 773-774, 1990.

97. Tager, I.B., "Health Effects of 'Passive Smoking' in Children," Chest 96(5): 1161-1164, 1989.

98. Sneddon, J.M. and Bearpark, T.M., "Indoor Air, Respiratory Health and Pulmonary Function in Children: A Critical Review." In: Indoor Air Quality and Ventilation. London, Selper Ltd., Volume 2, 143-154, 1990.

99. Witorsch, R.J. and Witorsch, P., "A Critical Analysis of the Relationship Between Parental Smoking and Pulmonary Performance in Children," Off Gesundh-Wes 51: 78-83, 1989.

100. Rubin, D. and Damus, K., "The Relationship Between Passive Smoking and Child Health: Methodologic Criteria Applied to Prior Studies," Yale Journal of Biological Medicine 61(5): 401-411, 1988.

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Response to Question 2a(iii) (continued):

Asthma

Asthmatics are sometimes believed to be particularly vulnerable to various environmental influences, including PTS, but the scientific data in this area are contradictory and inconclusive. Most of these studies have been conducted neither in the home nor in the workplace but are clinical studies that have potential applicability to either setting. There are ten major studies on the possible association of exposure to PTS and acute respiratory symptoms in adult nonsmokers.[1-10] The studies are inconsistent in their reported results, and the authors often fail to adequately control for confounding factors. Furthermore, the authors often cannot rule out the possibility of psychological factors playing a role in the reported reactions of asthmatics to PTS.

A Discussion of the Published Studies

A 1981 study by Dahms, et al., reported decreases in the pulmonary function of several asthmatics exposed to environmental tobacco smoke.[1] However, the study suffers from several obvious limitations, including the unrealistic conditions under which the subjects were exposed to PTS; they were challenged with high levels of smoke in an enclosed smog chamber. In addition, as the authors themselves noted, their experiment lacked proper controls, and the

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effects observed may have been due to psychological, not physical, factors.

Contrary to Dahms, et al., a Canadian group, Pimm, et al., observed no systemic lung changes among asthmatics exposed to levels of tobacco smoke typically found in public places.[2] Later research by the co-authors of this study supports this conclusion.[3] They reported that respiratory data collected from a group of asthmatic volunteers exposed to tobacco smoke "do not suggest that asthmatic subjects have an unusual sensitivity" to such exposure. Although several volunteers claimed to have experienced wheezing and tightness in the chest due to the exposure, the researchers determined that the "physiological data give little support to the concept of a subgroup with particular sensitivity." They noted that these reactions probably were due to the "suggestibility" of the subjects.

The difficulty in determining the impact of psychological responses in such studies is clearly demonstrated by the results of two reports from Australia. Although a 1985 report by Knight and Breslin suggests that short-term PTS exposures are capable of inducing reactions in asthmatics,[4] an earlier study co-authored by Breslin tends to support the theory that psychological reactions may partially explain symptoms observed during such exposures.[5] In that study, Breslin and Ing reported that although asthmatics

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exposed to tobacco smoke complained of subjective symptoms, no significant objective evidence of airways obstruction was observed.

Other studies also fail to provide support for claims regarding a relationship between PTS exposure and reactions in asthmatics. For example, Wiedemann, et al., at Yale University, examined the possible short-term effects of PTS exposure on a group of young asthmatic patients and observed no changes in lung flow rates.[6] They concluded that such exposures present "no acute respiratory risk" to asthmatics.

Tulane University scientists, Stankus, et al., recently assessed the effects of heavy exposure to PTS in a group of self-reported "tobacco smoke-sensitive" asthmatics.[7] They reported that two-thirds of the subjects did not experience significant changes in pulmonary function even after heavy, prolonged exposure to PTS, and that there was no association between reactions to PTS and hypersensitivity to tobacco leaf extract, which is commonly used in allergy testing.

A report by Lebowitz on data from a large-scale epidemiological study in the U.S. suggests that PTS in the home does not affect symptoms or pulmonary function in either children or adult asthmatics, but that dust and pollen in the home apparently can provoke such effects.[8] Another group of U.S. researchers,

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Bailey, et al., also recently reported that exposure to PTS did not impair lung function in 263 asthmatic adult subjects.[9] A German research group, led by Magnussen, reported that one hour of exposure to PTS with 20 ppm carbon monoxide did not provoke acute respiratory symptoms or changes in lung function in 18 asthmatic adult subjects.[10]

Conclusion

The studies available on the reported association between adult asthma and exposure to PTS are inconclusive. The studies reporting an association suffer from several methodological problems. First, confounding factors are not adequately controlled for in many of the studies. Second, some of the studies report on inadequate sample sizes. Third, psychological factors have not been ruled out. Finally, a few of the clinical studies rely on unrealistic exposure conditions in enclosed smog chambers.

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REFERENCES

1. Dahms, T.E., Bolin, J.F. and Slavin, R.G., "Passive Smoking Effects on Bronchial Asthma," Chest 80(5): 530-534, 1981.

2. Pimm, P.E., Shephard, R.J. and Silverman, F., "Physiological Effects of Acute Passive Exposure to Cigarette Smoke in Asthmatics," Federal Proceedings 36(3): 606, 1977. Abstract.

3. Shephard, R.J., Collins, R. and Silverman, F., "'Passive Exposure of Asthmatic Subjects to Cigarette Smoke," Environmental Research 20: 392-402, 1979.

4. Knight, A. and Breslin, A.B.X., "Passive Cigarette Smoking and Patients with Asthma," The Medical Journal of Australia 142: 194-195, 1985.

5. Ing, A. and Breslin, A.B.X., "The Effect of Passive Cigarette Smoking on Asthmatic Patients," Proceedings, The Thoracic Society of Australia, 543, October, 1983. Abstract.

6. Wiedemann, H.P., Mahler, D.A., Loke, J., Virgulto, J.A., Snyder, P. and Matthay, R.A., "Acute Effects of Passive Smoking on Lung Function and Airway Reactivity in Asthmatic Subjects," Chest 89(2): 180-184, 1986.

7. Stankus, R.P., Menon, P.K., Rando, R.J., Glindmeyer, H., Salvaggio, J.E. and Lehrer, S.B., "Cigarette Smoke-Sensitive Asthma: Challenge Studies," Journal of Allergy and Clinical Immunology 82: 331-338, 1988.

8. Lebowitz, M., "The Effects of Environmental Tobacco Smoke Exposure and Gas Stoves on Daily Peak Flow Rates in Asthmatic and Non-Asthmatic Families." In: ETS-Environmental Tobacco Smoke: Report from a Workshop on Effects and Exposure Levels. R. Rylander, Y. Peterson and M.-C. Snella (eds.). Published simultaneously in European Journal of Respiratory Diseases, Supplement No. 133, Vol. 65, 90-97, 1984.

9. Bailey, W.C., Richards, J.M., Manzella, B.A., Brooks, C.M., Windsor, R.A. and Soong, S.J., "Characteristics and Correlates of Asthma in a University Clinic Population," Chest 98(4): 821-828, 1990.

10. Magnussen, H., "The Effect of Passive Smoking on Airway Tone and Responsiveness in Children and Adults with Bronchial Asthma," The Toxicology Forum: 1990 European Meeting, Budapest, Hungary. June 18-22, 1990: 202-205.

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Response to Question 2a(iii) (continued):

Allergy

Although some individuals are annoyed by the sight and smell of tobacco smoke and a few even report experiencing irritation, the existence of human allergens in tobacco smoke has not been established scientifically.

A number of research groups have been unable to conclude that humans actually experience a true tobacco smoke allergy.[1-6] In 1980, for example, a group of researchers noted that "direct evidence that tobacco smoke is immunogenic [capable of evoking a specific response] in man is yet to be documented."[5] A more recent report by this same group affirms this conclusion.[6]

Claims about a human tobacco allergy stem primarily from studies in which tobacco leaf extract has been reported to cause allergic skin responses in some people, usually in those who already experience allergic reactions to other substances such as weeds.[7-9] However, as an English immunologist pointed out, there are "great difficulties" in determining whether positive reactions to tobacco leaf extracts are relevant to clinical responses to tobacco smoke.[4] Although he noted that there may be substances in tobacco smoke which could "theoretically" act as such agents, he concluded that

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"there is no proof that the specific sensitization to tobacco smoke exists."

It has also been hypothesized that tobacco smoke is capable of provoking an asthma attack as an allergic reaction.[10-11] However, a Swedish specialist concluded that such results are not proof of a tobacco allergy because the studies, which used tobacco extracts, did not differentiate between non-specific and true allergic reactions in evaluating the results of skin tests and bronchial provocation.[12] Consequently, he stated, "for the present, the question as to whether allergy to cigarette smoke exists or not should be kept open." Other research affirms this point. Scientists reported in 1988 that tobacco leaf sensitivity was not associated with decreased pulmonary function in allergic asthmatics.[13]

Certainly, there appear to be people who may be sensitive to tobacco smoke, but personal annoyance and emotional reactions should not be confused with genuine allergic reactions. In many cases, the individual may be responding to high room temperatures, lack of ventilation, or even to the mere sight of tobacco smoke. Indeed, Dr. John Salvaggio, the director of an allergic disease center in the U.S., has suggested that reported reactions to tobacco smoke may be irritative rather than allergic. After reviewing the studies on the allergy question, he concluded that "there is no

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proof that tobacco smoke is allergenic in man."[14]

Accordingly, it is not surprising that researchers at the Mayo Clinic failed to find any evidence of tobacco smoke allergies in their tests of subjects who considered themselves allergic to tobacco and tobacco smoke.[15] It has been reported in other studies that people who claim to be "smoke sensitive" did not react more frequently to tobacco leaf or smoke extract than those who are "smoke resistant."[13,16]

On the basis of these data, it must be questioned what people really mean when they say they are "allergic" to tobacco smoke. It may be that they simply do not like the sight and smell of tobacco smoke and are interpreting their reaction to mean that they are "allergic" to environmental tobacco smoke. But, as has been pointed out, such personal reactions should <u>not</u> be regarded as true tobacco smoke allergies.

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REFERENCES

1. Justus, D. and Adams, D., "Evaluation of Tobacco Hypersensitivity Responses in the Mouse: A Potential Animal Model for Critical Study of Tobacco Allergy," Int Arch Allergy Appl Immunol 51(6): 687-695, 1976.

2. Lehrer, S., et al., "Immunochemical Properties of Tobacco Smoke and Leaf Components," Fed Proc 37(6): 1456, 1978.

3. Lehrer, S., et al., "Immunogenic Properties of Tobacco Smoke," J Allerg Clin Immunol 62(6): 368-370, 1978.

4. Taylor, G., "Tobacco Smoke Allergy -- Does It Exist?" In: Environmental Tobacco Smoke Effects on the Nonsmoker: Report from a Workshop. R. Rylander (ed.). Published in Scand J Respir Dis Supplement 91: 50-55, 1974.

5. Lehrer, S., et al., "Immunogenicity of Tobacco Smoke Components in Rabbits and Mice," Int Arch Allergy Appl Immunol 62: 16-22, 1980.

6. Lehrer, S., et al., "Tobacco Smoke Sensitivity: A Result of Allergy?," Ann Allergy 56: 1-10, 1986.

7. Gleich, G., et al., "Allergy to Tobacco Antigens," J Allerg Clin Immunol 63(3): 211-212, 1979.

8. Harkavy, J., "Tobacco Allergy in Cardiovascular Disease: A Review," Ann Allerg 26: 447-459, 1968.

9. Speer, F., "Tobacco and the Nonsmoker: A Study of Subjective Symptoms," Arch Environ Health 16(3): 443-446, 1968.

10. Stahle, I. and Tibbling, L., "Tobaksallergi hos Patienter Med Asthma Bronchiale (Tobacco Allergy Among Patients with Bronchial Asthma)," Lakartidningen 75(17): 1711-1713, 1978. Translation.

11. Tibbling, L., "Elicitation of Bronchial Asthma with Tobacco Extract." In: Abstracts of the 4th World Conference on Smoking and Health. Stockholm, Sweden, June 18-21, 1979.

12. Bylin, G., "Tobaksallergi -- finns den? (Tobacco Allergy -- Does It Exist?)," Lakartidningen 77(16): 1530-1532, 1980. Translation.

13. Stankus, R. and Lehrer, S., "Inhalation Challenge Studies on Tobacco Smoke Sensitive Asthmatics." In: Indoor and Ambient

2046157615

Source: https://www.industrydocuments.ucsf.edu/docs/qnwl0000

Air Quality. R. Perry and P. Kirk (eds.). London, Selper Ltd., 303-304, 1988.

14. Salvaggio, J., Statement, U.S. Congress Committee on Agriculture, Subcommittee on Tobacco, Effect of Smoking on Nonsmokers, Hearing, 95th Congress, 2nd Session, Washington, D.C., U.S. Government Printing Office, 46-49, September 7, 1978.

15. McDougall, J. and Gleich, G., "Tobacco Allergy -- Fact or Fancy?," J Allerg Clin Immunol 57(3): 237, 1976. Abstract.

16. Lehrer, S., et al., "Immunological Evaluation of Tobacco Smoke 'Sensitive' Individuals by Skin, Radioallergosorbent and Precipitin Tests," J Allerg Clin Immunol 67: 49, 1981. Abstract.

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PHILIP MORRIS RESPONSE TO OSHA RFI

Question 2a(iv): "What data are available that associate adverse health effects with exposure to radon?"

Summary:

Radon, a naturally occurring radioactive gas, is ubiquitous in the indoor environment. Epidemiologic studies report an increased risk of lung cancer associated with the inhalation of radon and its radioactive "daughters" in underground miners. Although questions remain about radon dosimetry, it has been suggested that radon may be associated with an increased risk of lung cancer in the general population. Radon levels in buildings may be reduced with adequate ventilation.

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PHILIP MORRIS RESPONSE TO OSHA RFI

Question 2a(iv): "What data are available that associate adverse health effects with exposure to radon?"

Response:

Epidemiologic studies report that the inhalation of radon progeny is associated with an increased risk of lung cancer among underground miners.[1,2] Because elevated radon levels have been measured in some residences, it has also been suggested that radon exposure may be responsible for between ten and 20 percent of the attributable lifetime lung cancer risk in the general population.[3,4]

Radon-222 is a naturally occurring radioactive gas, ubiquitous in both outdoor and indoor environments, produced by the radioactive decay (breakdown) of uranium; radon itself decays, producing "progeny" or "daughters," which, along with radon itself, may be inhaled.[2] Some of the progeny, namely the isotopes polonium-214 and -218, have short half-lives, meaning that they may decay while in the lungs, emitting alpha particles that then impact on lung tissue.[5] Radon progeny have been described as the most important source of natural irradiation in the general population.[3,6]

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Questions remain about radon dosimetry and lung cancer risk.[2] For instance, some have claimed that radon exposure and cigarette smoking interact to increase the risk of lung cancer.[7] Models of the purported interaction include multiplicative (synergistic), additive and submultiplicative models. However, Jacobi and Paretzke, using a modified proportional hazard model, adapted to account for relevant epidemiological data, concluded that the relative fractions of radon-related lung cancer rates could be nearly the same for smokers and nonsmokers.[8]

With regard to epidemiologic studies, Harley and Pasternack wrote that[9]

> [t]he problem of attributable risk where smoking and radon daughter exposures are combined cannot be resolved at present. . . One recent study of Swedish iron miners which has nearly complete follow-up to death shows evidence that the attributable risk in smoking miners is about the same as in nonsmoking miners. That is, the 'extra' risk from radon daughters is the same whether the individual smokes or not.

Elsewhere, Harley notes that in one miner study[10]

> Radford and Renard found that the excess lung-cancer rate in nonsmokers was as high as in smokers with equivalent radiation exposure. When the actual rate of lung cancer was compared with the expected rate, the ratio was higher in nonsmokers than in smokers, per unit of radiation exposure.

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Furthermore, in a case-control study of 292 female lung cancer cases in the city of Stockholm, Sweden, Svensson and colleagues[11] reported a relative risk of 2.2 for lung cancer associated with "living in dwellings close to the ground in areas with an increased risk of radon emanation." Nevertheless, they also reported that smoking habits were not a major confounder of the reported association.

Moreover, at least one animal inhalation study reported that the incidence of lung tumors was less in beagle dogs exposed to cigarette smoke and radon progeny:[12]

> [C]igarette-smoke exposure, under the conditions of the experiment, had a mitigating effect on radon-daughter-induced respiratory cancer in dogs.

(Four groups of dogs were exposed as follows: to radon, radon daughters, and uranium ore dust; to radon, radon daughters, uranium ore dust and cigarette smoke; to cigarette smoke only; or to room air.) The authors proposed that increased mucus production in the smoking dogs was the best explanation for the small number of respiratory tumors in that group.[13]

With regard to "passive" tobacco smoke (PTS), it has been suggested that PTS can affect the dosimetry of indoor radon

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by modifying the behavior of its decay products (progeny).[14] Because airborne particles (e.g., from smoke or dust) provide sites for attachment, their presence may reduce the "unattached" fraction of radon progeny, i.e., the free ions produced in the decay process. (The "attached" fraction consists of progeny present on larger (around 130 nm; 1 nm equals 1/1,000,000,000 of a meter, or approximately 4/100,000,000 of an inch) airborne particles.) Because the progeny in the "unattached" fraction are around 3 nm in size, they are thought to deposit more efficiently in the respiratory tract, particularly in the bronchial rather than the pulmonary regions. It has been estimated that the dose reduction when PTS is present in the air may be as much as 35%. Moreover,[15]

> [A] combination of many factors have to be considered when calculating the uptake and retention of various pollutants, and . . . airborne concentration information is simply insufficient to properly develop population risk estimates. Added to this, individual differences in physique, breathing pattern, deposition, clearance and metabolism may also occur.

In a recent study, Stebbings and Dignam measured total radon body burden (i.e., the level of external and internal radon contamination), and reported a "clear negative association between current smoking and the presence of high radon daughter contamination levels" in their study subjects [emphasis added].[16] The authors noted:

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This does not directly support the relationship assumed in the current literature that passive smoking increases lung dose by increasing the equilibrium ratio. The latter may occur, but there may be stronger countervailing factors, such as reduction of superficial plateout.

Furthermore, the University of Pittsburgh Radon Project included over 73,000 radon measurements in homes and reported that radon levels tended to be lower in smokers' homes than in nonsmokers' homes.[17] The researchers suggested that smokers might tend to open windows more often (i.e., increasing ventilation), which could influence radon levels.

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REFERENCES

1. Ellett, W.H. and Nelson, N.S., "Epidemiology and Risk Assessment: Testing Models for Radon-Induced Lung Cancer." In: Indoor Air and Human Health. R.B. Gammage and S.V. Kaye (eds.). Chelsea, Michigan, Lewis Publishers, Inc., 79-107, 1985.

2. Guilmette, R.A., Johnson, N.F., Newton, G.J., Thomassen, D.G. and Yeh, H.C., "Risks from Radon Progeny Exposure: What We Know, and What We Need to Know," Annual Review of Pharmacology and Toxicology 31: 569-601, 1991.

3. International Commission on Radiological Protection, "Lung Cancer Risk from Indoor Exposures to Radon Daughters," Acta Oncologica 26: 489-490, 1987.

4. Maher, E.F., Rudnick, S.N. and Moeller, D.W., "Effective Removal of Airborne 222Rn Decay Products Inside Buildings," Health Physics 53: 351-356, 1987.

5. Nero, A., "Earth, Air, Radon and Home," Physics Today 32-39, April 1989.

6. Hewitt, C.N. and Kelly, M., "Environmental Radon: A Brief Review," Environmental Technology 11: 387-392, 1990.

7. Samet, J.M. and Nero, A.V., "Indoor Radon and Lung Cancer," The New England Journal of Medicine 320: 591-594, 1989.

8. Jacobi, W. and Paretzke, H.G., "Risk Assessment for Indoor Exposure to Radon Daughters," The Science of the Total Environment 45: 551-562, 1985.

9. Harley, N.H. and Pasternack, B.S., "Response to 'Application of Epidemiologic Methods to the Study of Radon and Lung Cancer,'" Health Physics 42: 734-735, 1982.

10. Harley, N.H., "Radon and Lung Cancer in Mines and Homes," The New England Journal of Medicine 319: 1525-1527, 1984.

11. Svensson, C., Eklund, G. and Pershagen, G., "Indoor Exposure to Radon from the Ground and Bronchial Cancer in Women," International Archives of Occupational and Environmental Health 59: 123-131, 1987.

12. Cross, F.T., Palmer, R.F., Filipy, R.E., Dagle, G.E. and Stuart, B.O., "Carcinogenic Effects of Radon Daughters, Uranium

2046157624

Source: https://www.industrydocuments.ucsf.edu/docs/qnwl0000

Ore Dust and Cigarette Smoke in Beagle Dogs," Health Physics 42: 33-52, 1982.

13. Gies, R.A., Cross, F.T. and Dagle, G.E., "A Histologic Study of the Influence of Cigarette Smoking in Suppressing Rn Daughter Carcinogenesis in Dogs," Health Physics 53: 327-329, 1987.

14. Pritchard, J.N. and Strong, J.C., "The Influence of Environmental Tobacco Smoke on Radon Dosimetry." In: Indoor Air '90: Proceedings of the Fifth International Conference on Indoor Air Quality and Climate. Toronto, Canada, Volume 3, 33-38, 1990.

15. McAughey, J.J., Pritchard, J.N. and Black, A., "Risk Assessment of Exposure to Indoor Air Pollutants," Environmental Technology 11: 295-302, 1990.

16. Stebbings, J.H. and Dignam, J.J., "Contamination of Individuals by Radon Daughters: A Preliminary Study," Archives of Environmental Health 43: 149-154, 1988.

17. Cohen, B.L. and Gromicko, N., "Variation of Radon Levels in U.S. Homes with Various Factors," JAPCA 38: 129-134, 1988.

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PHILIP MORRIS RESPONSE TO OSHA RFI

Question 2(d): "Based on observations in your workplace or your knowledge from other sources, how much lost work time and decreased productivity may be traceable to illnesses relating to poor indoor air quality? What is the basis for your estimate?"

Summary:

Several studies in the scientific literature on indoor air quality suggest that poor indoor air quality is related to lost work time and decreased productivity. Insofar as poor indoor air quality is associated with inadequate ventilation, the literature indicates that an increase in ventilation to rates specified in ASHRAE Standard 62-1989 may improve productivity and reduce absenteeism rates. The cost incurred in an increase in outdoor air ventilation is, according to these authors, offset by increased worker morale, productivity and reduced absenteeism.

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PHILIP MORRIS RESPONSE TO OSHA RFI

Question 2(d): "Based on observations in your workplace or your knowledge from other sources, how much lost work time and decreased productivity may be traceable to illnesses relating to poor indoor air quality? What is the basis for your estimate?"

Response:

A number of estimates and examples of lost work time and decreased productivity attributable to poor indoor air quality are found in the published literature. For example, Professor James Woods has estimated that a 25 percent energy savings in building operations (e.g., reduced ventilation) may be out-weighed by the loss of anywhere from 2 to 6 minutes per person per day of productive concentration.[1]

A 1990 report issued by the United States Air Force estimates the following:[2]

> The cost of personnel in the Air Force averages about $250.00 per square foot per year. The maintenance and energy costs for all operations in a building rarely exceed $7.00 per square foot per year. Of the $7.00, no more than $2.00 are energy costs. If the unlikely proved true and we saved half of all energy costs by running closed or minimum fresh air cycles, that would be $1.00/sq ft/yr. This is the equivalent of seven hours per square foot of personnel time. This is less than two minutes per day per year. If only two minutes per day

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productive time is lost, then all energy savings are wiped out. Respiratory disease is at least 1.5 to 3 times more likely in a tight environment. Common respiratory infection episodes last eight to ten days with one to two days of absence being usual. The average number of respiratory infections involving colds and flu is one per person per year based on National Center for Health Statistics data. Tight buildings are likely to raise that number to between 1.5 and 3.0 episodes per person per year. Using the lower figure of one day of loss per episode, we have raised the lost days from one to between 1.5 and 3 per person per year with an average of 2.25 days. This is an average increase of 1.25 days. By this measure alone we have lost 10 hours, three more than is required to put us in the deficit column. Three of the days of infection are likely to suffer from reduced productivity by at least 20% for a total of 60% of a day. Cost is now 1.85 excess days lost; 1.85/220 = 0.84% x $250/sq ft/yr = $2.10/sq ft/yr. This cost already exceeds the savings possible by running the air handler with inadequate fresh air by 2.1 times. This analysis does not begin to address the losses due to aggravation of pre-existing problems such as asthma and allergies, the cost of other diseases known to result from improper maintenance and operation of air handlers, the loss in productivity due to irritant effects of poorly controlled 'comfort' parameters or the losses due to the social atmosphere surrounding the problems generated. The actual savings from running closed cycle are even less than the generous $1.00 we allowed. It is usually necessary to increase total outside added air from roughly 10% of total flow to obtain adequate fresh air and control CO_2 to appropriate levels. If all of the $2.00 were going to climate control, this represents only 20 cents rather than a dollar in savings. Since this is so, the actual relative loss from increase in infections is $2.10/0.20 = 10.5 times the possible energy savings if all energy is used for heating. This is a poor bargain.

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In testimony before the United States Congress in 1991, a representative from the Sheet Metal and Air Conditioning Contractors National Association, Inc., (SMACNA) reported on a study conducted in which building energy cost simulations at two levels of ventilation were evaluated. In the study, outside air intake was increased 50 percent and the estimated increase in energy cost was $1,800.00 on an annual basis. According to SMACNA, the same study "compared the cost of absent or sick workers affected by unhealthy ventilation and concluded that increased ventilation cost 1/135 of the cost of absent and sick employees."[3]

In another 1991 publication, Mr. Peter Binnie describes a hypothetical situation where energy costs for maintaining acceptable IAQ are considered in terms of employee absentee rates. He writes:[4]

> Consider the following situation. In a typical building of 100,000 square feet, the move from 20 cubic feet per minute (10 litres per second) of fresh air per person down to, say, 5 cubic feet per minute (2.5 litres per second) per person may on average result in cost savings of perhaps $20,000 per annum. This could represent a 40% savings in the energy costs associated with ventilation, or 10-15% of the building's overall energy budget. Everyone in upper management would be pleased, and one can be certain that future years' budgets would be reduced to reflect the actual costs of this first year. Thus, the building is now doomed to function with no more than 5 cubic feet per minute (2.5 litres per second) per person. As HBI, ASHRAE and many others have found, this

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action results in unacceptable indoor pollution and increased absentee rates.

In the United States and Europe, offices are commonly staffed with a generous average of 150 square feet of space per employee. Thus, in the hypothetical building of 100,000 square feet, there would be 67 staff. If they are paid the minimum wage of $15,000 per annum, the payroll bill would reach $10 million per annum. This means that every 1% of absenteeism would cost $100,000 per annum. Surely a decision to save $20,000 per year on energy that results in reducing worker productivity and increasing absentee rates involving hundreds of thousands of dollars in costs is poor business judgment.

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REFERENCES

1. Kreiss, K., "The Sick Building Syndrome: Where Is the Epidemiologic Basis?," AJPH 80(10): 1172-1173, 1990.

2. Carpenter, D. and Poitrast, B., "Recommended Carbon Dioxide and Relative Humidity Levels for Maintaining Acceptable Indoor Air Quality," USAF Occupational and Environmental Health Laboratory, Brooks AFB, Texas: October, 1990.

3. The Sheet Metal and Air Conditioning Contractors' National Association, Inc., Statement on HR 1066 to The House Science, Space and Technology Committee Environment Subcommittee, May 9, 1991.

4. Binnie, P., "The Role of Ventilation in Controlling the Quality of Indoor Air, Including ETS." In: Other People's Tobacco Smoke. A. Armitage (ed.). E. Yorks, U.K., Galen Press, 159-172, 1991.

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PHILIP MORRIS RESPONSE TO OSHA RFI

Question 3(a): "What correlation, if any, can be made between symptoms presented and IAQ complaints and type of causative agent? For example, are certain symptoms more indicative of exposure to chemical contaminants as opposed to biological contaminants? Please give examples.

(b) If such a correlation has been made, how effective is this information in identifying sources of contaminants?"

Summary:

Four large databases on sick-building syndrome investigations, including databases from NIOSH, Health and Welfare Canada, T.D. Sterling and Associates, Ltd., and Healthy Buildings International, do not reveal significant correlations between IAQ complaints and symptoms and specific types of causative agents. In over 50 percent of all sick-building cases, symptoms and complaints are abated by increasing ventilation to levels comparable to those specified in ASHRAE 62-1989. In addition, the four databases indicate that complaints and symptoms can be correlated to tobacco smoking in only two to four percent of all sick-building investigations.

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PHILIP MORRIS RESPONSE TO OSHA RFI

Question 3(a): "What correlation, if any, can be made between symptoms presented and IAQ complaints and type of causative agent? For example, are certain symptoms more indicative of exposure to chemical contaminants as opposed to biological contaminants? Please give examples.

(b) If such a correlation has been made, how effective is this information in identifying sources of contaminants?"

Response:

The scientific literature contains a number of studies on "sick building syndrome," a condition which gives rise to a number of complaints, including headaches, nausea, coughs, sore eyes and breathing difficulties. Research also indicates that this complex pattern of symptoms is commonly reported in modern office buildings whether or not smokers are present.[1,2,3,4,5,7,8]

The reported findings of several Canadian investigators demonstrate this point. In 1983, two of these researchers reported on their extensive review of over 150 indoor air quality evaluations of office buildings compiled by U.S. government agencies, universities and others.[5] After examining the data collected during these evaluations, they concluded that smoking did not significantly

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affect either indoor atmospheres or the frequency of worker complaints and symptoms:

> The review of available studies does not provide any objective evidence that either pollution levels or patterns of health related complaints differ in some remarkable way between locations with or without smoking restrictions.

They did observe that "inadequate" ventilation creates conditions "where discomfort and illness result irrespective of whether or not smoking is permitted." These observations were reaffirmed in reports published in 1987 and 1989.[4,6] In their 1989 report, the researchers noted that smoking was related to complaints in only 12 of 408 (less than three percent) of the building investigations included in the database.

Government investigators with Health and Welfare Canada (HWC), in their report on 94 building studies, also noted that only five percent of the complaints were attributable to indoor constituents such as photocopy machine emissions and PTS.[3] In a 1990 update, these investigators reported on data from a total of 1,362 building investigations. Inadequate ventilation was identified as a problem in 52 percent of the buildings.[7]

Similarly, researchers with the U.S. National Institute of Occupational Safety and Health (NIOSH), in a review of 203 air

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quality investigations of government and business offices, schools and health care facilities, concluded that tobacco smoke played a contributing role in only four (two percent) of the building complaints investigated.[1] A large majority of the complaints were traced to general building contamination and inadequate ventilation. Recently, NIOSH officials reported on an additional 326 building investigations conducted by the agency through 1988.[8] Over one-half of the investigations revealed inadequate ventilation as the source of complaints.

In 1988, a representative of a U.S. firm specializing in the maintenance of office air conditioning and heating systems reported on 223 individual indoor air quality investigations of publicly and privately owned office buildings.[2] As in the NIOSH investigations, PTS was implicated in only four percent of the buildings investigated. He stated that the majority of indoor air quality problems in modern office buildings may be traced to inadequate fresh air circulation and to poorly maintained ventilation systems which act as breeding grounds for fungi, bacteria and other contaminants. He also suggested that visible tobacco smoke ought to be considered a symptom, rather than a cause, of general indoor air quality problems, in that PTS is often the only visible sign that a ventilation problem exists.

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In 1990, investigators from the same firm reported on a survey of 26 commercial office buildings in 20 cities in Switzerland.[9] Unacceptably low ventilation rates were reported in more than half of the buildings investigated. PTS was associated with complaints in only six buildings, all of which also were affected by inadequate ventilation. Acceptable ventilation rates, according to the researchers, resulted in low levels of PTS constituents.

It is perhaps understandable, given the easy recognition of PTS, that persons experiencing sick building symptoms tend to blame PTS. Indeed, researchers have indicated that the mere visibility or presence of tobacco smoke may provoke claims that PTS is the cause of reported symptoms and complaints.[10,11] However, removal of PTS through smoking bans may serve only to divert attention from more basic, underlying indoor air quality problems. As one commentator pointed out: "Removing the smoker entirely, then, may not affect health and comfort problems in 95% to 98% of sick buildings."[12]

Other published studies in the literature tend to support conclusions from the four major databases on sick building syndrome. For example, in 1989, Hedge, et al., reported on an investigation of indoor air quality and health complaints in two office buildings with different ventilation systems.[13] While the researchers noted

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that self-reports of exposure to PTS were associated with an increase in perceived symptom prevalence, they also observed that no significant correlations between PTS constituents, as measured in the office areas, and symptom prevalence could be found.

A 1991 report by Hawkins and Wang[14] ranked a number of variables related to self-reported symptoms of sick building syndrome. Those variables included (from "most frequently" to "least frequently" reported): "humidity," "satisfaction with work," "active smoking," "gender," "exposure to PTS," "office light," and "doing professional work." They concluded:

> Building Sickness Score was associated with many factors. Sick building syndrome symptoms are influenced by multiple variables of which the environmental factor of humidity and the psychological factors of work, sex, and occupation are important.

In another 1991 report, Hedge, et al., observed that "in an ongoing study of the effects of smoking policy on IAQ and SBS in air conditioned offices, no evidence of substantial IAQ differences have been found in nonsmoking open plan offices in 15 buildings with various kinds of restrictive smoking policies or 3 buildings that prohibit smoking. To date, 3,155 workers in these offices have been surveyed and results show that, contrary to expectations, workers in the smoking-prohibited buildings on average

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report more symptoms than in those buildings with a restrictive smoking policy."[15]

The same investigators also noted that other research by Valbjorn, et al. in 1990 "found that samples from supply ducts in 13 ventilation systems contained from 70 to 6,200 viable fungi per gram of dust and from 50 to 5,000 viable bacteria per gram of dust. Samples from ventilation filters also contained 70 to 3,400 fungi per gram of dust and 100 to 6,700 viable bacterial per gram of dust. Dust in ventilation supply ducts was found to be similar to that sampled from the floor. Ghazi (1990) reports that removal of dust mite feces from carpets in an office resulted in a 25% reduction in SBS symptoms."[15]

In 1983, Sterling and co-workers reported on a number of sick building investigations in which symptoms were directly related to (1) detergent residues, (2) fibrous glass dust from duct work, (3) formaldehyde off-gassing from insulation, (4) photo-chemical smog formation and (5) viable organisms located in duct systems, cooling towers and humidification chambers.[16]

Indoor air quality in schools has recently become an issue of considerable concern. In 1989, Helsing and co-workers reported the results of an IAQ investigation in a school.[17] They reported that "there was an insufficient fresh air supply to some

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classrooms, and a large percentage of students exhibited classic symptoms of Sick-Building Syndrome, i.e., headache, eye burning, fatigue. Correcting the ventilation problems resulted in reduction of symptoms to a level approximately equal to that of students in other schools in the county."

Similarly, investigations by Hanssen (1987)[18] and Beller (1989)[19] reported that low air exchange rates in combination with installation of new building materials was the main cause of complaints in the schools they investigated.

Norback and colleagues have published a number of investigations on sick building syndrome. In a 1987 report, the researchers compared groups of individuals reporting SBS symptoms and noted that while "SBS-symptoms were not uncommon among non-exposed reference groups, a remarkable over frequency of SBS-symptoms were demonstrated among the SBS-groups in this investigation."[20] Neither atopy (a predisposition toward the development of allergies) nor smoking habits could explain their observation. In a 1989 follow-up report, the researchers reported that "the sick building groups did not differ from the reference groups with regard to other factors such as mean age, smoking habits, atopy frequency, work stress, or work satisfaction."[21] In still another investigation, the research group reported on a sick building investigation in which the removal of wall-to-wall carpets

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resulted in a decrease in reported systems to a level similar to those in individuals without previous or current exposure to carpeting.[22]

A 1989 report by Dr. James Woods assesses 30 cases of "problem buildings" investigated by the Honeywell Corporation since 1986.[23] Woods' research indicates that 75% of the buildings investigated had inadequate outdoor supply air intake. Similarly, 75% of the buildings had inadequate air distribution to occupied spaces, and 75% of the buildings suffered from inadequate maintenance protocols.

Kim (1990) summarized investigations of 105 problem buildings by Clayton Environmental Consultants. She wrote:[24]

> In a survey of 105 problem buildings, Clayton found that 53 percent had maintenance problems, 49 percent had operational problems (such as improper handling of control equipment), and 33 percent had design problems. Mechanical engineers evaluated the HVAC systems in 70 of the buildings, in which they found that 75 percent had maintenance problems, 70 percent had operational problems, and 47 percent had design problems. Of the 105 buildings, 95 were sampled for contaminants. Of these 28 were found to have problem levels of microbial contaminants, 26 had volatile organic compounds, and 13 had combustion products.

In 1987, Burge and co-workers reported on symptoms of building sickness among 4,373 office workers in 42 different office

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buildings and under 47 different ventilation conditions in the United Kingdom.[25] They reported that the most common work-related symptoms were lethargy, blocked nose, dry throat and headache. These symptoms increased substantially once the supply air was either chilled or humidified. In a similar study in Denmark, Skov and colleagues examined sick building syndrome reports in 4,369 office workers.[26] Their research indicated that indoor climate perception was strongly related to the prevalence of SBS symptoms. Lifestyle factors were only weakly associated with the reporting of symptoms.

Canadian researchers recently reported results of a building investigation which included measurements of temperature, humidity, dust, nicotine, formaldehyde, volatile organic compounds and CO_2.[27] Occupants of the building complained of poor indoor air quality and questionnaire evaluation revealed a substantial number of complaints about unsatisfactory thermal comfort, dry air, drowsiness and eye irritation. However, all measured parameters, including temperature and humidity, were within accepted comfort and exposure guidelines. The authors were unable to correlate any single measured environmental parameter with complaints and symptoms. They concluded that their investigation "showed that complaints reported by the occupants were associated with perceived rather than measured levels of indoor environmental parameters."

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In summary, reported exposures to PTS have been directly associated with sick building syndrome complaints in only 2 to 4 percent of the buildings investigated.[1-8] Because it is easily identifiable in the indoor environment, PTS is often blamed for IAQ problems. However, recent research by Winneke and colleagues suggests that an individual who is predisposed to annoyance from PTS will be more likely under experimental exposure conditions to respond with annoyance symptoms.[11] A NIOSH psychologist, Dr. Michael Colligan, offers an explanation for this kind of response. He writes:[28]

> It appears then, that the individual is sensitive to fluctuations in the functioning of the autonomic nervous system. When perceived changes in his subjective state are understandable, e.g., 'I have an allergy,' 'I've been under a lot of pressure to met a deadline,' 'I'm worried about my teenager,' an individual can initiate various coping strategies to deal with the causes. When the origins of the experienced distress are vague or unclear, however, an individual starts searching around for salient cues. If the environment provides a plausible cause in the form of a pungent odor or dense, stuffy air, then an individual can conclude, rightly or wrongly, that the poor quality of the environment is responsible for his physical and psychological discomfort. Notice that this process can occur independently of any specific toxic effects the environment might have on the individual and irrespective of the 'real' cause of the autonomic arousal. All that is required is that an individual experience autonomic arousal in response to a subtle or unidentified stressor or combination of stressors. Cues provided by the environment

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in the form of noxious odors, visually detectable particulates or dust, or humid, stuffy air, may suggest to an individual that his discomfort is a toxic response to an airborne pollutant. That environment then becomes a source of threat to the individual, which in turn may generate more autonomic arousal and anxiety.

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REFERENCES

1. Melius, J., et al., "Indoor Air Quality -- the NIOSH Experience," Ann Am Conf Gov Ind Hyg 10: 3-7, 1984.

2. Robertson, G., "Source, Nature and Symptomology on Indoor Air Pollutants." In: Indoor and Ambient Air Quality. R. Perry and P. Kirk (eds.). London, Selper Ltd., 311-319, 1988.

3. Kirkbride, J., Sick Building Syndrome: Causes and Effects, Health and Welfare Canada, Ottawa, Canada, October 24, 1985.

4. Collett, C. et al., "A Database of Problem Buildings: Learning by Past Mistakes." In: Present and Future of Indoor Air Quality. C. Bieva, et al. (eds.). Amsterdam, Elsevier Science Publishers, 413-419, 1989.

5. Sterling, T. and Sterling, E., "Investigations on the Effect of Regulating Smoking on Levels on Indoor Pollution and on the Perception of Health and Comfort of Office Workers." In: ETS - Environmental Tobacco Smoke: Report from a Workshop on Effects and Exposure Levels. R. Rylander, Y. Peterson and M.C. Snella (eds.). Published simultaneously in European Journal of Respiratory Diseases, Supplement No. 133, Vol. 65, 17-31, 1984.

6. Sterling, T., et al., "Environmental Tobacco Smoke and Indoor Air Quality in Modern Office Work Environments," Journal of Occupational Medicine 29(1): 57-62, 1987.

7. Kirkbride, J., et al., "Health and Welfare Canada's Experience in Indoor Air Quality Investigation." In: Indoor Air '90: Proceedings of the Fifth International Conference on Indoor Air Quality and Climate. Toronto, Canada, Volume 5, 99-106, July 29-August 3, 1990.

8. U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health, Division of Standards Development and Technology Transfer, "The NIOSH Approach to Conducting Indoor Air Quality Investigations in Office Buildings," Indoor Air Quality Selected References, September, 1989.

9. Turner, S. and Binnie, P., "An Indoor Air Quality Survey of Twenty-Six Swiss Office Buildings." In: Indoor Air '90: Proceedings of the Fifth International Conference on Indoor Air Quality and Climate. Toronto, Canada, Volume 4, 27-32, July 29-August 3, 1990.

2046157646

Source: https://www.industrydocuments.ucsf.edu/docs/qnwl0000

10. Pimm, P., et al., "Physiological Effects of Acute Passive Exposure to Cigarette Smoke," Arch Environ Health 33(4): 201-213, 1978.

11. Winneke, G., et al., "Psychophysiological Response to Environmental Tobacco Smoke in an Experimental Social Setting." In: Indoor Air Quality. H. Kasuga (ed.). Berlin, Heidelberg, Springer-Verlag, 173-183, 1990.

12. Sterling, T. and Kleven, S., "The Epidemiology of 'Sick Public Buildings'." In: Indoor Air Quality: Symposium. Buenos Aires, National Academy of Sciences of Buenos Aires, 79-96, 1989.

13. Hedge, A., et al., "Indoor Air Quality and Health in Two Office Buildings with Different Ventilation Systems," Environmental International 15: 115-128, 1989.

14. Hawkins, L. and Wang, T., "The Office Environment and the Sick-Building Syndrome," Healthy Buildings 365-371, 1991.

15. Hedge, A., et al., "Breathing-Zone Filtration Effects on Indoor Air Quality and Sick Building Syndrome Complaints," Healthy Buildings 351-357, 1991.

16. Sterling, T.D., et al., "Building Illness in the White-Collar Workplace," International Journal of Health Services 3: 277-287, 1983.

17. Helsing, K.J., et al., "Cure of a Sick Building: A Case Study," Environmental International 15: 107-114, 1989.

18. Hanssen, S. and Mathisen, H., "Sick Building -- A Ventilation Problem?," Indoor Air '87, Proceedings of the 4th International Conference on Indoor Air Quality and Climate, Berlin (West), 17-21 August 1987, Institute of Water, Soil and Air Hygiene 3: 357-361.

19. Beller, M. and Middaugh, J., "Results of an Indoor Air Pollution Investigation," Alaska Medicine 31(4): 148-155, 1989.

20. Norback, D., et al., "Overfrequencies of Skin and Airway Symptoms Among Personnel In Sick Buildings and Polluted Industrial Environments in Relation to Exposure," Indoor Air '87, Proceedings of the 4th International Conference on Indoor Air Quality and Climate, Berlin (West), 17-21 August 1987, Institute of Water, Soil and Air Hygiene 2: 515-519.

21. Norback, D., et al., "The Prevalence of Symptoms Associated with Sick Buildings and Polluted Industrial Environments as Compared to Unexposed Reference Groups Without Expressed

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Dissatisfaction," Environment International 15: 85-94, 1989.

22. Norback, D. and Torgen, M., "A Longitudinal Study Relating Carpeting with Sick Building Syndrome," Environmental International 15: 129-135, 1989.

23. Woods, J., "Cost Avoidance and Productivity in Owning and Operating Buildings," Occupational Medicine 4: 753-771, 1989.

24. Kim, I., "Sick Building Syndrome: M.E.'s Seek a Cure," Mech Engineering 112: 53-54, November, 1990.

25. Burge, S., et al., "Sick Building Syndrome: A Study of 4373 Office Workers," Ann Occup Hyg 31: 493-504, 1987.

26. Skov, P., et al., "Influence of Personal Characteristics, Job-Related Factors and Psychosocial Factors on the Sick Building Syndrome," Scand J Environ Health 15: 286-295, 1989.

27. Haghighat, F., et al., "Relationship Between Occupant Discomfort as Perceived and as Measured Objectively," Indoor Environ 1: 112-118, 1992.

28. Colligan, M., "The Psychological Effects of Indoor Air Pollution," Bulletin of the New York Academy of Medicine 57: 1014-1026, 1981.

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PHILIP MORRIS RESPONSE TO OSHA RFI

Question 3a

Appendix: Press Reports of "Sick Building Syndrome"

The attached Appendix volumes contain press reports of specific incidents of "sick building syndrome." Complaints from occupants in these buildings have been traced to a number of sources, including: high levels of volatile organic compounds, bacteria, mold, spores, plumbing, roof and air conditioning leaks, high heat, excessive humidity and general unsanitary conditions. Consistent with NIOSH data, few, if any, complaints were related to tobacco smoke. In fact, smoking is prohibited in many of these buildings.

Occupants reported symptoms and complaints ranging from allergies and malaise to pneumonia and death. In some cases, the cause was never actually identified, yet building occupants continue to experience symptoms. Some workers have been forced to change employment or were unable to continue working at all.

The attached reports represent but a small sample of affected buildings in the U.S. Building types include public and private office buildings, schools, hotels, hospitals, courthouses, child care centers, retirement homes and even a homeless shelter.

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For ease of reference, a state-by-state listing of the buildings identified in these illustrative, published reports is attached.

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BUILDINGS THAT ARE REPORTEDLY SICK

Volume I

State	City	Building
AK	Anchorage	State Office Building
AK		Indoor skating rink
AZ	Tucson	Amelia Maldonado Elementary School
CA	Anaheim	Pacific Volt
CA	Beverly Hills	The Beverly Plaza Hotel
CA	Burbank	Lockheed Corp.
CA	Chino	California Institution for Men
CA	Duarte	City of Hope Medical Center
CA	El Segundo	El Segundo Airport Towers, Building C
CA	Goleta	Raytheon Co.
CA	Hayward	Helen Turner Child Care Center
CA	Jackson	Amador County Courthouse, District Attorneys Office
CA	Los Angeles	UCLA Medical Center
CA	Los Angeles	Westwood Horizons residential facility
CA	Oakland	Merritt-Peralta Medical Center
CA	Oakland	Alameda County Courthouse
CA	Poway	Midland Elementary School
CA	Richmond	Social Security Administration
CA	Richmond	Richmond Health Center
CA	Sacramento	Bateson Building (State Office Building)

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State	City	Building
CA	Sacramento	Twin Towers -- State Office Buildings CA Depts. of Health Services & Social Services
CA	San Diego	San Diego County Courthouse
CA	San Diego	Income Property Group Office Park Building
CA	San Francisco	Bancroft-Whitney Co.
CA	Stanford	Stanford University Medical Center
CA	Sunnyvale	Lockheed Missile and Space Co.
CA	Westwood	Wadsworth Veterans Administration Medical Center
CA		Lakeside Village Condominiums
CO		Susquehanna Building
CO	Castle Rock	Douglas County School District Administrative Offices
CO	Denver	Federal Building
CO	Lamar	Best Western Cow Palace
CO	Rocky Flats	Rocky Flats Nuclear Weapons Plant (U.S. Department of Energy)
CO	Westminster	City Pool
CT	Bristol	Police - Court Complex
CT	Hartford	Bulkeley High School
CT	Hartford	One Myrtle Street
CT	Hartford	U.S. Post Office
CT	New Britain	New Britain High School
CT	New Haven	Hospital of St. Raphael

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State	City	Building
CT	New Haven	Yale Medical School, Dept. of Epidemiology and Public Health
CT	Stamford	West Main Street Shelter
CT		Connecticut insurance company
		Volume II
DC		EEOC Headquarters
DC		U.S. Dept. of Interior
DC		U.S. Information Agency
DC		General Services Administration Building
DC		White House
DC		SSA Payment Center
DC		Parklawn Building, U.S. Dept. of HHS
DC		Madison Building, Library of Congress
DC		EPA Headquarters Waterside Mall
DC		U.S. Housing and Urban Development Building
DC		Frances Perkins Building, U.S. Labor Dept.
DC		Hubert Humphrey Office Building
DC		National Museum of American History, Smithsonian Institution
FL		South Florida Savings & Loan
FL	Bartow	Polk County Courthouse

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State	City	Building
FL	Deerfield Beach	House of Insurance
FL	Ft. Lauderdale	Broward County Hospital
FL	Ft. Lauderdale	South Florida Savings Bank
FL	Ft. Lauderdale	Broward County School
FL	Ft. Lauderdale	Broward County Library
FL	Ft. Lauderdale	Paragon Building
FL	Ft. Lauderdale	Broward County Airport Control Center
FL	Gainesville	Veterinary School, Univ. of Florida
FL	Kissimmee	The Hyatt - Orlando Hotel
FL	Lauderdale Lakes	Lauderdale Lakes City Hall
FL	Lauderhill	Lauderhill Mall, State of Florida Offices
FL	Oakland Park	Northridge Medical Plaza, V.A. Clinic
FL	Pensacola	Escambia County Dept. of Public Health
FL	University Station	John and Grace Allen Administration Building University of South Florida
FL	West Palm Beach	City Hall
FL	West Palm Beach	Palm Beach County Governmental Center
FL	Ybor City	Lozano Building Hillsborough County Environmental Protection Commission
GA	Atlanta	101 Marietta Tower Bldg.
IL	Chicago	Wrigley Building

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State	City	Building
IL	Chicago	Social Security Administration Bldg.
IN	Evansville	St. Mary's Medical Center
IN	Indianapolis	Methodist Hospital
IN	Russiaville	West Elementary School
IN		Indiana office complex
IA	Iowa City	University of Iowa Hospitals
IA	Ottumwa	Wapello County and Iowa Depts. of Human Services Building
KS	Belleville	Agricultural Stabilization and Conservation Services; Soil Conservation Service USDA Agencies
KS	Wichita	Pioneer TeleTechnologies
KY	Bowling Green	Richardsville Elementary School
LA	Baton Rouge	Pleasant Hall, Louisiana State University
LA	Bogalusa	Winn-Dixie Grocery Store
ME		Maine Department of Transportation
MD	Bethesda	Bethesda Naval Hospital
MD	College Park	University of Maryland
MD	Hagerstown	Western Maryland Center State Hospital
MD	Rockville	U.S. Public Health Service Building
MD	Waldorf	Thomas Stone High School
MD	Woodlawn	U.S. Health Care Financing Administration, Meadows East Building

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State	City	Building
MD	Woodlawn	City Office Building
	Volume III	
MA	Andover	West Elementary School
MA	Boston	Metropolitan State Hospital
MA	Boston	Cambridge Rindge & Latin High School
MA	Norwood	Polaroid
MI	Detroit	Madison Center (Court Building)
MI	Detroit	Airport Hilton Inn
MI	Pontiac	Oakland County Complex
MO	Centralia	Temple Industries Inc.
MO	Jefferson City	Truman State Office Building
MT	E. Helena	Tri-Valley Credit Union Building
NE	Lincoln	Federal Building
NV	Carson City	State Capitol Building
NV	Lake Tahoe	Harvey's Wagon Wheel
NH	Concord	Beaverbrook Elementary School
NH	Nashua	New Searles Elementary School
NJ	Atlantic City	Bally's Park Place Hotel and Casino
NJ	Flemington	Hunterdon Central Regional High School
NJ	Mahwah	Municipal Offices
NJ	Mahwah	Ramapo College

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State	City	Building
NJ	Red Bank	Bell Communications Research Building
NM	Albuquerque	Social Security Administration
NY	Albany	Building 8, State Office Campus Department of Taxation and Finance
NY	Brooklyn	Downstate Medical Center
NY	Hudson County	Whitney Young Elementary School
NY	NYC	General Services Administration
NY	NYC	New York Times Company
NY	NYC	Brandeis High School
NY	Rochester	Eastman Kodak
NY	Rochester	Rochester General Hospital
NY	Schenectady	Wappingers Falls High School
NY	Wappingers Falls	Van Wyck Junior High School
OH	Cincinnati	Alms & Doepke Building
OH	Cincinnati	Goodall Building
OH	Cincinnati	Office Building
OH	Columbus	Northland Terrace Nursing and Rehabilitation Center
OH	Dayton	Wright Patterson Air Force Base
OK	Muskogee	CH Haskell Building, Oklahoma State University
PA	Harrisburg	Sporting Hill Elementary School
PA	Philadelphia	Social Security Administration
RI	Providence	Rhode Island Hospital

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State	City	Building
TN	Nashville	Tennessee State Museum
TN	Nashville	Metro Courthouse
TN	Nashville	Nashville Federal Building
TN	Nashville	Artista Records Nashville Headquarters
TX	Austin	Texas Dept. of Housing and Community Affairs
TX	Austin	Austin Hospital
TX	Austin	Texas Board of Pardons and Paroles
TX	Dallas	Ferrell Center, Baylor Univ.
TX	Dallas	Polish Power, Inc.
TX	Houston	Johnson Space Center - NASA
TX	Houston	Judwin Properties Apartment Complexes
TX	Wimberly	Elementary School
UT		VA Hospital
UT	Moab	State Social Services Office Building
UT	Ogden	IRS Service Center
VT	Burlington	University of Vermont College of Medicine
VA	Blacksburg	Cowgill Hall-Virginia Tech
VA	McLean	Franklin Sherman Elementary School
VA	Richmond	Montrose Elementary School
VA	Richmond	Office Building
VA	Arlington	USA Today Headquarters

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State	City	Building
VA	Springfield	West Springfield High School
VA	Suffolk	Human Resources Building
WA	Kettle Falls	Kettle Falls High School
WA	Monroe	Monroe Reformatory, Washington Dept. of Corrections
WA	Seattle	Harbourview Medical Center
WA	Seattle	John Hay Elementary School
WA	Seattle	Snohomish County Courthouse
WA	Spokane	City Public Safety Building
WA	Tacoma	Highrise office building
WV	Welch	Mount View High School
WI	Eau Claire	Holiday Inn
WI	Green Bay	Brown County Mental Health Center
WI	Milwaukee	West Milwaukee School District
WI	Milwaukee	809 Building
WI	Port Washington	Ozaukee County Courthouse
WI	Sheboygan	Plastics plant
WI	Traux	Madison Area Technical College

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PHILIP MORRIS RESPONSE TO OSHA RFI

Question 5: "In cases where IAQ investigations have identified a bioaerosol as the etiologic cause of a building-related illness:

(a) Did complaints occur within a specific length of time?

(b) Were there similarities in symptoms among affected individuals which suggested exposure to a specific agent, e.g., Legionella pneumophila? Was the etiological agent identified?

(c) What laboratory tests were performed to confirm that a specific bioaerosol was responsible for health complaints?

(d) How was the problem resolved?"

Summary:

A review of some published case studies of health effects related to biological contamination of the indoor environment provides some insight into the process of identifying specific biological agents related to those health effects. Outbreaks of various diseases and illnesses have been correlated with improper maintenance or operation of ventilation systems, suggesting that proper maintenance and operation could reduce the incidence of bioaerosol-related illness. Specifically, Legionella, the causative agent of both Legionnaires' disease and Pontiac fever, has been detected in cooling towers and water systems. Microbial contamination of humidifiers and of previously flooded areas has been associated with humidifier fever and hypersensitivity pneumonitis.

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PHILIP MORRIS RESPONSE TO OSHA RFI

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(a) Did complaints occur within a specific length of time?

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(c) What laboratory tests were performed to confirm that a specific bioaerosol was responsible for health complaints?

(d) How was the problem resolved?"

Response:

A review of some published case studies of health effects related to biological contamination of the indoor environment provides some insight into the process of identifying specific biological agents related to those health effects.

Legionnaires' Disease

The outbreak which gave Legionnaire's disease its name occurred during an American Legion Convention at the Bellevue Stratford Hotel in Philadelphia, PA, in 1976.[1] A total of 221 cases were identified; there were 34 deaths. After a six-month investigative process, the bacterium Legionella pneumophila was

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identified as the causative agent from samples of lung tissue.[2] The outbreak was linked to airborne dissemination of bacteria via the hotel's ventilation system.[1]

A 1978 outbreak of 15 cases of L. pneumophila pneumonia at Baptist Memorial Hospital in Memphis, TN, is also often discussed in the literature.[3,4,5] This epidemic coincided with the use of an auxiliary cooling unit that had not been used for two years. Legionella had proliferated in the tower; when it was operated, Legionella-containing aerosol drifted into and was dispersed by the hospital ventilation system.

O'Mahony, et al., report on their investigation of an English police headquarters building where six cases of Legionnaires' disease were reported.[6] They used a case-control design to find the main area of the building associated with the infection (the cases worked in a communications wing and the controls elsewhere in the building). Microbiological investigations of cooling system water and sludge implicated cooling tower drift and exhaust. Interestingly, sick building syndrome symptoms (influenza-like illnesses and other minor complaints) were also associated with working in the communications wing. Remediation procedures included draining and disinfecting the cooling tower, resiting the ventilation system air intake away from the cooling

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tower exhaust, and eventually switching to an air-cooled ventilation system.

In September 1991, 13 cases (one fatal) of Legionnaires' disease were diagnosed among 1,200 employees at a Social Security Administration building in Richmond, CA.[7] Investigators reportedly found Legionella in a basement sink, water fountains, elevator shafts and two of the building's five cooling towers. One case of Legionnaires' disease was also diagnosed in 1991 at the IRS Service Center in Ogden, UT.[7]

Pontiac Fever

In 1968, during a one-week period, 95 of 100 employees contracted a flu-like illness at an Oakland County Health Department building in Pontiac, MI.[3,4,5,8] There was an association between development of the illness and presence in the building when the air-conditioning system was operating. Exhaust from an evaporative condenser was found to be located near the intake of another ventilation system. At the time of the outbreak, the etiologic agent could not be identified, but was eventually traced to Legionella, when that organism was identified following the 1976 Legionnaires' disease outbreak in Philadelphia. This outbreak and several outbreaks of Legionnaires' disease have been traced to airborne transmission of bacteria.[9]

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Hypersensitivity Pneumonitis and Humidifier Fever

Finnegan and Pickering correlate the development of hypersensitivity pneumonitis (HP) with the presence of contaminated humidifiers.[5] In one case, four of 27 office workers developed either progressive dyspnea or the symptoms of HP (intermittent chills, fever and shortness of breath while at work). With regard to humidifier fever, in one workplace, 12 of 17 workers showed systemic or respiratory symptoms after exposure to a contaminated humidifier. The symptoms stopped when their exposure to humidifiers stopped and re-appeared when exposure began again; therefore, this led to the conclusion that the humidifier was the source of the causative agent.

In a 1988 review, Morey and Feeley report on several case studies.[10] In one, a large office building had repeated floods and other "water disasters." More than 25% of the occupants exhibited symptoms of humidifier fever. An amoeba (Acanthamoeba polyphaga) and a bacterium (Thermoactinomyces) were isolated; these have been associated with hypersensitivity lung disease elsewhere. Nevertheless, because of sampling difficulties, the etiologic agent in this case could not be conclusively identified. In another case, one occupant of an office was being treated for a respiratory infection caused by Pseudomonas aeruginosa. This bacterium was

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not found in a sample taken after the office portable humidifier had been turned off for at least twelve hours. However, a "dramatic" elevation in indoor bacteria followed within a few minutes after the humidifier was turned on, suggesting that the source of the infection-causing bacteria was the humidifier.

Laboratory tests

Tests may be performed on samples to isolate specific agents.[11] Culture media may be used to isolate individual types of organisms, by providing certain nutritional requirements specific to the species. Collected aerosols may be examined using antigen analysis when a causal organism is strongly suspected and when specific antibodies are available, e.g., in the case of HP or humidifier fever. Specific analyses for toxins, e.g., endotoxin are being developed.

The Enzyme Linked Immuno-Sorbent-Assay (ELISA) inhibition test is useful in identifying airborne allergens.[12] Also, the RadioImmunoSorbent Test (RAST), an in vitro method, can be used to assess allergenicity.[13]

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REFERENCES

1. American Society of Heating, Refrigerating and Air-Conditioning Engineers, Inc., Legionellosis Position Statement/Legionellosis Position Paper, ASHRAE, Atlanta, GA, 1989.

2. Winn, W.C., "Legionnaires Disease: Historical Perspective," Clinical Microbiology Reviews 1: 60-81, 1988.

3. Imperato, P.J., "Legionellosis and the Indoor Environment," Bulletin of the New York Academy of Medicine 57: 922-935, 1981.

4. LaForce, F.M., "Airborne Infections and Modern Building Technology," Environment International 12: 137-146, 1986.

5. Finnegan, M.J. and Pickering, C.A.C., "Review: Building Related Illness," Clinical Allergy 16: 389-405, 1986.

6. O'Mahony, M., Lakhani, A., Stephens, A., Wallace, J.G., Youngs, E.R. and Harper, D., "Legionnaires' Disease and the Sick-Building Syndrome," Epidem Inf 103: 285-292, 1989.

7. Wallace, B., "No Proof Yet of Source of Legionnaire's Disease," The San Francisco Chronicle, A12, September 21, 1991.

"Bacteria Keeps Building Closed," Los Angeles Times, A27, September 21, 1991.

"Second Suspected Outbreak of Legionnaire's Disease Demands Massive Government Intervention, Union Chicago," PR Newswire, September 20, 1991.

Johnson, C., "Legionnaire's Disease Cleanup Moving Slowly, Federal Office May Be Closed Three Weeks," The San Francisco Chronicle, A20, September 20, 1991.

"Legionnaire's Disease Cases Reach Nine," The Associated Press, September 19, 1991.

"Legionnaires' Cases at Building Rise to 9," Los Angeles Times, September 19, 1991.

Johnson, C., "8th New Case of Legionnaire Disease Found," The San Francisco Chronicle, A17, September 19, 1991.

Goodavage, M., "Workers Fear Return to 'Sick Building,'" USA Today, 3A, September 20, 1991.

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Source: https://www.industrydocuments.ucsf.edu/docs/qnwl0000

8. Bardana, E.J., Montanaro, A. and O'Hollaren, M.T., "Building-Related Illness: A Review of Available Scientific Data," Clinical Reviews in Allergy 6: 61-89, 1988.

9. Blackmon, J.A., Chandler, F.W., Cherry, W.B., England, A.C., Feeley, J.C., Hicklin, M.D., McKinney, R.M. and Wilkinson, H.W., "Legionellosis," American Journal of Pathology 103(3): 427-465, 1981.

10. Morey, P.R. and Feeley, J.C., "Microbiological Aerosols Indoors, in Workplaces, Schools, and Homes," ASTM Standardization News Dec. 1988: 54-58, 1988.

11. Burge, H.A., "Bioaerosols: Prevalence and Health Effects in the Indoor Environment," The Journal of Allergy and Clinical Immunology 86: 687--701, 1990.

12. Elixmann, J.H., Linskens, H.F., Schata, M. and Jorde, W., "Can Airborne Fungal Allergens Pass Through an Air-Conditioning System?" Environment International 15: 193-196, 1989.

13. van Bronswijk, J.E.M.H., Rijckaert, G. and van de Lustgraaf, B., "Indoor Fungi, Distribution and Allergenicity," Acta Bot. Neerl. 35: 329-345, 1986.

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PHILIP MORRIS RESPONSE TO OSHA RFI

Question 6: "IAQ investigations conducted by NIOSH indicate that some type of biological contaminant was involved in five percent of the cases.

(a) Are there other data available which indicate the prevalence of biological contaminants as the cause of adverse health effects?

(b) Are data available which indicate the likelihood that health complaints are related to a specific bioaerosol contaminant? If so, please indicate the source of such data."

Summary:

Publicly available statistics indicate that a substantial portion (around 40%) of buildings may have biological contamination. Some 8-10% of pneumonia cases in the United States may be due to Legionella, a bacterium often found in water-containing components of ventilation systems. Large numbers of individuals may experience symptoms of asthma or sick building syndrome, or may become ill with colds or flu; such conditions affect their ability to work and result in health care and other costs. For instance, some researchers estimate that overall costs related to respiratory illnesses in the United States may reach into the billions of dollars. Bioaerosol contamination of ventilation systems and subsequent illness among exposed persons is thus a major concern.

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PHILIP MORRIS RESPONSE TO OSHA RFI

Question 6: "IAQ investigations conducted by NIOSH indicate that some type of biological contaminant was involved in five percent of the cases.

(a) Are there other data available which indicate the prevalence of biological contaminants as the cause of adverse health effects?

(b) Are data available which indicate the likelihood that health complaints are related to a specific bioaerosol contaminant? If so, please indicate the source of such data."

Response:

Prevalence of Building Complaints Referable to Bioaerosols

A recent article in Healthy Buildings International (HBI) magazine stated that in Honeywell's Indoor Air Quality Diagnostics group's investigation of 51 commercial office buildings between 1986 and 1990, microbial contamination was considered a factor in 41% of the cases.[1] Similarly, HBI's own investigation of over 700 buildings identified 43% with microbial contamination (34% fungal, 9% bacterial).

The state of California instituted a telephone log to track complaints received by its indoor air quality program.[2] Calls

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to this program suggested that 16% of building occupants with a complaint perceived that biological contamination was a problem.

Bardana, et al., reference other sources of data on building investigations in addition to NIOSH: the Centers for Disease Control has investigated 12 building-associated disease outbreaks between 1978 and 1981, and the State of Oregon Department of Human Resources (Health Division) has investigated 11 since 1984.[3] They also note a number of investigations sponsored by state agencies, including the State Department of Transportation building, Augusta, ME; the Health Service Center, Sandpoint, ID; the Human Services building, Holland, MI; the NBC offices, New York, NY; the Gregory Bateson Building, Sacramento, CA; the Social Services building, San Francisco, CA; and Oakland High School, Oakland, CA.

Prevalence of Diseases/Symptoms Referable to Bioaerosols

Burge and Hodgson report that 8-10% of community-acquired pneumonias are attributable to Legionella.[4] Case-fatality rates are approximately 15%, making these bacteria "a major contributor to mortality in the U.S.: an estimated 5,000 to 7,000 deaths per year." In the 85% of non-fatal cases, legionellosis has a "substantial financial burden through time lost from work and additional health care costs." These authors also estimate costs related to episodes of viral respiratory disease in the range of

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150 million work days and $59 billion. With regard to allergic asthma, which may be exacerbated by bioaerosols, they estimate that 3% of the U.S. population (9,000,000 persons) has this condition. Of 135,000 hospital admissions yearly, averaging 8 days and costing 5,000,000 work days per year, approximately 15% are due to allergic disease. Burge and Hodgson find the data on HP to be less well-established. Two studies of office workers suggested that workers reported symptoms consistent with HP at rates of 1.2 or 4%. Similarly, humidifier fever complaint rates are reportedly in the area of 2-3%.

Tamblyn and colleagues recently reported that various surveys had reported that the prevalence of nasal problems among workers in mechanically-ventilated office buildings was 22-62% and cough was 18-41%.[5] In their own survey of four buildings for fungal spore content, the prevalence of weekly respiratory and mucosal irritation symptoms among 1,627 persons ranged from 24-47%.

Burge tabulates available statistics on the indoor transmission of respiratory diseases.[6] She estimates that 800,000,000 persons suffer a respiratory illness each year (many of these influenza and the common cold), with an estimated total cost of $24,000,000,000. With the "conservative" estimate that 10% are due to IAQ, a cost of $750,000,000 is attributed to indoor air quality. For Legionnaires' disease, she estimates 20,000

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community and 200,000 hospital cases each year, with about 36,000 deaths. 90% would be related to IAQ. Burge also states that at least 35,000 deaths per year can be attributed to airborne infectious disease; related costs are over $1 billion. Influenza results in 400 million days of restricted activity (almost 2 days per person per year). 53-71% of infected adults have lower respiratory symptoms, resulting in lost work time and hospitalization.

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REFERENCES

1. Anonymous, "Biological Pollutants in the Indoor Environment," Healthy Buildings International Magazine Sept./Oct. 1991: 10-13, 1991.

2. Macher, J.M., "Inquiries Received by the California Indoor Air Quality Program on Biological Contaminants in Buildings." In: Advances in Aerobiology. Basel, Birkhauser Verlag, 275-278, 1987.

3. Bardana, E.J., Montanaro, A. and O'Hollaren, M.T., "Building-Related Illness: A Review of Available Scientific Data," Clinical Reviews in Allergy 6: 61-89, 1988.

4. Burge, H.A. and Hodgson, M., "Health Risks of Indoor Pollutants," ASHRAE Journal 30: 34-36, 38, 1988.

5. Tamblyn, R.M., Menzies, R.I., Comtois, P., Hanley, J., Tamblyn, R.T., Farant, J.P. and Marcotte, P., "A Comparison of Two Methods of Evaluating the Relationship Between Fungal Spores and Respiratory Symptoms Among Office Workers in Mechanically Ventilated Buildings." In: IAQ 91: Healthy Buildings. Atlanta, American Society of Heating, Refrigerating and Air-Conditioning Engineers, Inc., 136-141, 1991.

6. Burge, H.A., "Risks Associated with Indoor Infectious Aerosols," Toxicology and Industrial Health 6: 263-274, 1990.

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PHILIP MORRIS RESPONSE TO OSHA RFI

Question 7: "Persons with underlying health problems or chemical sensitivities often cannot work in industries where physical strength and endurance or exposure to chemicals occur in the normal job experience.

(a) Is there evidence to suggest that these persons are more susceptible to developing health effects due to short-term exposure to PTS, such as eye and respiratory tract irritation?

(b) Is there evidence to suggest that these persons are more susceptible to developing health effects due to long-term exposure to PTS, such as cardiovascular disease and lung cancer?"

Summary:

There is a growing controversy in the medical community over the nature and extent of a physiological condition known as multiple chemical sensitivity (MCS). Conventional physicians and "clinical ecologists" disagree on the origins of the alleged sensitivities. Many conventional physicians appear to believe that the condition may be of a psychological origin. We are unaware of any original data on whether people allegedly afflicted with MCS are at increased risk of long-term health effects associated with exposure to various indoor air constituents. There are reports in the scientific literature, however, that people supposedly afflicted with MCS are more reactive and sensitive to short-term exposures to a wide range of indoor air constituents, outdoor air constituents, food additives and water contaminants. Authors of various studies have reported that adequate ventilation and focusing on indoor air in its entirety will help avoid symptoms of MCS allegedly due to tight building syndrome.

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PHILIP MORRIS RESPONSE TO OSHA RFI

Question (7): "Persons with underlying health problems or chemical sensitivities often cannot work in industries where physical strength and endurance or exposure to chemicals occur in the normal job experience.

(a) Is there evidence to suggest that these persons are more susceptible to developing health effects due to short-term exposure to PTS, such as eye and respiratory tract irritation?

(b) Is there evidence to suggest that these persons are more susceptible to developing health effects due to long-term exposure to PTS, such as cardiovascular disease and lung cancer?"

Response:

We are unaware of any studies reporting original scientific data on persons allegedly afflicted with multiple chemical sensitivity (MCS). This is due, in part, to the fact that there is not a widely accepted definition of the condition (e.g., as Hileman wrote, "there is a lack of a clear definition of what it [MCS] is").[1] A second author offered the following possible definition of MCS:[2]

> Multiple chemical sensitivities (MCS) is an acquired disorder characterized by recurrent symptoms, referable to multiple organ systems, occurring in response to demonstrable exposure to many chemically unrelated compounds at doses far below those established in the general

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population to cause harmful effects. No single widely accepted test of physiologic function can be shown to correlate with symptoms.

Probably the most heated debate, however, centers on whether MCS is a psychological condition, a physiological condition, or both.[1-2] Hileman wrote the following regarding this controversy:[1]

> To many traditional allergists and psychiatrists, the onset of MCS is due almost entirely to psychological factors. Some consider the syndrome to be a variant of somatoform disorder (the conversion of mental experiences into bodily symptoms) or of posttraumatic stress disorder. Others say that the root problem is an irrational belief on the part of the patients that chemicals are making them sick. . . Other physicians -- and these are likely to be clinical ecologists and some traditional physicians who practice occupational medicine -- believe that chemical exposures are causing these people to be ill. They think so because of common threads they see in the clinical histories of these patients.

Terr wrote the following in her critique of clinical ecology theories and practice:[3]

> The concept of multiple chemical hypersensitivities as a disease entity in which the patient experiences numerous symptoms from numerous chemicals and foods caused by a disturbance of the immune systems lacks a scientific foundation. Published reports of such cases are anecdotal and without proper controls. There is no convincing evidence for any immunologic abnormality in these cases.

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> Diagnostic methods have been shown to be unreliable. Diagnosis, treatment, and theoretical concepts underlying the purported disease are not consistent with current immunologic knowledge and theory. As defined and presented by its proponents, multiple chemical hypersensitivities constitutes a belief and not a disease.

Brodsky wrote the following regarding the continuing controversy in the medical field:[4]

> The clinical ecology subculture, like earlier medical subcultures, is the product of patient concerns that the medical establishment cannot allay by treatment or by reassurance. For social and behavioral scientists, it represents a 'natural' experiment that can be studied. For those physicians who believe that clinical ecology is without scientific basis generally and/or that its practitioners interpret laboratory results incorrectly, it is a challenge and an irritant. The clinical ecologist-physician feels rejected and the victim of bias and unfair attack. The patient in this subculture feels that finally he has found someone who understands him and is trying to help him, but that he must pay the price of being disapproved or rejected by his former physicians.

In fact, Hileman wrote that "a large part of the medical profession has become so convinced of the ineffectiveness of clinical ecologists' therapies that physicians who suggest to patients ideas or treatments that are uniquely associated with clinical ecology risk being disciplined by their local medical boards."[1] However, MCS has been "legitimized in a number of federal and state

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government regulations and proposed bills."[1] The Social Security Administration also recognizes MCS, but the agency requires a case-by-case analysis of this illness before it will allow payment of disability.[1]

What is MCS?

Hileman describes MCS as follows:[1]

> As a group, people allegedly suffering from MCS have a large number and range of symptoms they attribute to chemical exposures. The complaints are physical and mental and involve nearly all the systems of the body. The most common symptoms include respiratory problems; headache; fatigue; flulike symptoms; mental confusion and short-term memory loss; gastrointestinal tract difficulties; cardiovascular irregularities; skin disorders; genitourinary problems; muscle and joint pains; irritability and depression; and eye, ear, nose, and throat problems. Some individuals experience only one symptom, but most have more than one.

She wrote that the "number of chemicals the victims respond to is equally wide." Hileman asserts that "in some of these complex mixtures it is hard to tell what, if anything, the patient is responding to." She stated the following regarding the specific circumstances that patients believe caused them to be afflicted with MCS:

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> Many patients can identify specific circumstances that initiated their illness. They say their problems began either after an overwhelming chemical exposure, such as a job-related chemical spill, or after a new, chronic, medium-level exposure, such as moving into a new house with significant emissions of volatile organic compounds from the building materials or beginning to work in a new building, often one with poor ventilation. Thereafter, the symptoms seem to wax and wane with low-level chemical exposures, and when exposures are avoided altogether, the symptoms abate or disappear. In an informal survey of some 6800 persons claiming to be chemically sensitive, conducted by a patient group called the National Foundation for the Chemically Hypersensitive, nearly half of the patients say their illness started with a pesticide exposure.

Hileman reports that, in the literature, people with MCS can be divided into four categories: 1) industrial workers; 2) tight building occupants; 3) contaminated communities; and 4) individuals. Ashford reports that two general types of exposure seem particularly able to initiate hypersensitivity: 1) "A massive, overwhelming exposure, such as a chemical spill, a fire involving synthetic materials, pesticide spraying, or working with chemicals in a confined, unventilated space"; and 2) "Repeated, low-level exposure to a complex array of synthetic organic compounds, as occurs with combustion products (such as diesel exhaust), tight buildings, and soldering."[5] Ashford wrote the following regarding "trigger" exposures in MCS:

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> At home, troublesome exposures for the chemically sensitive patient include the gas stove, one of the most commonly identified triggers of symptoms in these patients; combustion products from gas- or oil-fired furnaces and space heaters, water heaters, and central air heating systems; sponge rubber bedding, padding, and upholstery; plastics (especially pliable odorous plastics such as shower curtains); insecticides; perfumes; paintings and decorating materials; fireplaces; cleaning agents; disinfectants; deodorizers; mothballs; cedar closets; newsprint and other printed materials; fabrics in clothing, bedding, and window coverings, especially synthetics or coated fabrics; particleboard; gasoline vapors from attached garages; and carpeting and carpet padding. Disinfectant liquids and sprays containing phenolics frequently provoke symptoms in these patients.

Ashford asserted that in the workplace, adequate ventilation is very important.[5] He cited a study that compared health problems in two office buildings, one fully air-conditioned and the other naturally ventilated. The authors reported that "sickness was significantly increased in the air-conditioned building versus the naturally ventilated building." Ashford also discussed the effects of indoor air pollution in the EPA headquarters in Washington, D.C. in 1987 and 1988. He reported that "an estimated 124 of 2,000 employees exposed to volatile off-gassing from the carpet became ill, exhibiting symptoms ranging from eye, nose, and throat irritation and breathing problems to nausea, headache, dizziness, difficulty in thinking, fatigue, and increased susceptibility to many exposures formerly tolerated."

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Cullen wrote the following regarding lack of adequate ventilation in office buildings:[2]

> Two other important and recently recognized clinical syndromes in occupational medicine also deserve mention vis à vis MCS: tight building syndrome and mass psychogenic illness. In the tight building syndrome, now occurring in epidemic proportion in modern offices and other work places, low levels of irritants combine with inadequate fresh-air intake and often low humidity to cause irritative symptoms often associated with CNS problems such as fatigue and poor concentration.

Mooser wrote that "while some individuals have developed MCS following tight building syndromes, the overwhelming majority has not."[6] He states that "the incidents are instructive, however, in that they provide evidence of the irritant effects of low-level exposures, as well as the variability of individual reactivity." He also wrote:

> Although the syndrome of multiple chemical sensitivities has received increasing attention in recent years, data concerning its prevalence among the general population is virtually non-existent. Lack of a common definition as well as the variability of symptoms and diagnostic criteria hamper this effort. Little data is available the characterizes the multiple chemical sensitive population, although incidence among females appears to be considerably higher. Further research is needed not only to better characterize the population but, more importantly, to evaluate potential triggering factors.

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Levin wrote the following regarding the etiologic considerations of "environmental illness":[7]

> The potential causal agent must be one that can realistically initiate an illness. If a patient whose history, physical findings, and laboratory results are consistent with a diagnosis of environmental illness described himself as completely well until he was exposed to the second-hand smoke of a single cigarette, another potential etiologic factor would be sought. If this patient described the onset of illness after a single exposure to an intensely toxic gas that is associated with severe acute symptoms, the toxic gas would be a candidate as the causal factor, since this is an etiologic agent that can reasonably cause disease.

He also wrote that "adequate ventilation of workplaces, utilization of appropriate protective clothing and respirators for workers, coupled with appropriate waste disposal techniques, will avoid contamination of workers and others with toxic chemicals and the spread of problems."

Summary

In summary, there are no original data on whether people allegedly afflicted with MCS are at increased risk of long-term health effects associated with exposure to various indoor air constituents. There are reports in the literature, however, that people reportedly afflicted with MCS are more reactive and

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REFERENCES

1. Hileman, B., "Multiple Chemical Sensitivity," C & EN July 22: 26-42, 1991.

2. Cullen, M.R., "The Worker with Multiple Chemical Sensitivies: An Overview," Occupational Medicine: State of the Art Reviews 2(4): 655-661, 1987.

3. Terr, A., "'Multiple Chemical Sensitivities': Immunologic Critique of Clinical Ecology Theories and Practice," Occupational Medicine: State of the Art Reviews 2(4): 683-694, 1987.

4. Brodsky, C., "Multiple Chemical Sensitivies, and Other 'Environmental Illness': A Psychiatrist's View," Occupational Medicine: State of the Art Reviews 2(4): 695-704, 1987.

5. Ashford, N.A. and Miller, C.S., "Chemical Exposures: Low Levels and High Stakes. Part I. Defining Chemical Sensitivity: Chapter 3. Origins of Multiple Chemical Sensitivity and Effects on Health," Chemical Exposures 0(0): 59-84, 1991.

6. Mooser, S.B., "The Epidemiology of Multiple Chemical Sensitivities (MCS)," Occupational Medicine: State of the Art Reviews 2(4): 663-668, 1987.

7. Levin, A.S. and Byers, V.S., "Environmental Illness: A Disorder of Immune Regulation," Occupational Medicine: State of the Art Reviews 2(4): 669-681, 1987.

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sensitive to short-term exposures to a wide range of indoor air constituents, outdoor air constituents, food additives, and water contaminants. Authors of various studies have reported that adequate ventilation and focusing on indoor air in its entirety will help avoid future cases of MCS allegedly due to tight building syndrome.

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PHILIP MORRIS RESPONSE TO OSHA RFI

Question 8: "Some people may develop an increased sensitivity to chemical pollutants, such as found in PTS, during pregnancy or treatment with certain medications (Calabrese 1978). What additional studies pertain to this sensitivity?"

Summary:

Calabrese (cited in OSHA RFI, reference #2) suggests that pregnant women and people on certain medications may develop an increased sensitivity to a wide-range of chemical substances. We are unaware of any other scientific studies regarding these alleged sensitivities. Contrary to the question above, Calabrese does not appear to implicate PTS per se as a specific agent related to these sensitivities. The author states that cadmium, lead, manganese, carbon monoxide, organophosphate insecticides, beryllium, fluoride, nitrogen dioxide, sulfur dioxide and ozone may potentially be associated with sensitivity reactions in some individuals. Although a few of these chemicals are reportedly found in tobacco smoke, there are numerous potential sources of these chemicals in the indoor environment.

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PHILIP MORRIS RESPONSE TO OSHA RFI

Question 8: "Some people may develop an increased sensitivity to chemical pollutants, such as found in PTS, during pregnancy or treatment with certain medications (Calabrese 1978). What additional studies pertain to this sensitivity?"

Response:

We are unaware of any other published studies that examine the sensitivities discussed by Calabrese in 1978. Furthermore, Calabrese does not appear to implicate PTS per se as a specific agent related to the sensitivities discussed in his paper. However, Calabrese does suggest that certain substances, including several that are sometimes found in the indoor environment, may be associated with sensitivity reactions among certain individuals.

Calabrese discusses developmental factors, genetic factors, dietary deficiencies, diseases, and behavioral factors that may predispose certain individuals to the possible toxic effects of environmental-occupational pollutants. The author provided charts of suspected pollutant agents and their possible health effects. PTS per se was not listed on these charts. Although several of the chemicals listed are reportedly found in

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tobacco smoke, there are numerous potential sources of these chemicals in the indoor environment.

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PHILIP MORRIS RESPONSE TO OSHA RFI

Question 11: "To your knowledge, have PTS exposures been associated with specific adverse health effects in humans?"

Response:

See Response to OSHA RFI Question 2a(iii) for a full discussion and critique of the literature on PTS exposures and reported associations between spousal (and parental) smoking and chronic/acute disease endpoints.

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PHILIP MORRIS RESPONSE TO OSHA RFI

Question 12: "To your knowledge, have PTS exposures been associated with specific adverse health endpoints in experimental animals?"

Summary:

Animal inhalation experiments using fresh sidestream smoke or constituents of sidestream smoke do not support the claim that PTS is a pulmonary carcinogen. Sidestream smoke is not equivalent to PTS, nevertheless, the two inhalation experiments using sidestream smoke that have been published reported no meaningful differences in the lung tissue of animals exposed to sidestream smoke and those not exposed to smoke. In addition, recent reviews of the literature on suspected pulmonary carcinogens have concluded that none of the individual constituents in sidestream smoke which are classified as potentially carcinogenic have been found to induce pulmonary cancer via inhalation in experimental animals.

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PHILIP MORRIS RESPONSE TO OSHA RFI

Question 12: "To your knowledge, have PTS exposures been associated with specific adverse health endpoints in experimental animals?"

Response:

Animal inhalation experiments using fresh sidestream smoke or constituents of sidestream smoke do not support the claim that PTS is a pulmonary carcinogen. Sidestream smoke is not equivalent to PTS, nevertheless, the two inhalation experiments using sidestream smoke that have been published reported no meaningful differences in the lung tissue of animals exposed to sidestream smoke and those not exposed to smoke. In one of the studies, German scientists exposed rats and hamsters to very high levels of sidestream smoke for a 90-day period; they reported no significant physiological effects on the tissues of the animals.[1] In the second study, researchers from the American Health Foundation exposed hamsters to sidestream and mainstream smoke for 18 months; they observed no significant increase in lung tumors among the animals exposed to sidestream smoke.[2,3,4]

In addition, recent reviews of the literature on suspected pulmonary carcinogens have concluded that none of the individual constituents in sidestream smoke which are classified as potentially

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carcinogenic have been found to induce pulmonary cancer via inhalation in experimental animals.[5,6]

Positive results reported for skin painting, intratracheal implantation or subcutaneous application in animals are of questionable relevance to the mode of exposure (inhalation) for PTS.

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REFERENCES

1. Adlkofer, F., et al., "Exposure of Hamsters and Rats to Sidestream Smoke of Cigarettes: Preliminary Results of a 90-Day-Inhalation Study." In: Indoor and Ambient Air Quality. R. Perry and P. Kirk (eds.). London, Selper Ltd., 252-258, 1988.

2. Haley, N., et al., "Uptake of Sidestream Smoke by Syrian Golden Hamsters," Toxicol Letters 35: 83-88, 1987.

3. Haley, N., "Sidestream Smoke Uptake By Syrian Golden Hamsters in an Inhalation Bioassay." In: Indoor Air '87: Proceedings of the 4th International Conference on Indoor Air Quality and Climate. Berlin, Volume 2, 68-73, August 17-21, 1987.

4. Hoffmann, D., American Health Foundation, "Experimental Tobacco Carcinogenesis: 2 PO1 CA29580-07, Subproject 6: Sidestream Smoke Carcinogenesis," Application for Continuation Grant to U.S. Department of Health and Human Services, Public Health Service, April 29, 1988.

5. Aviado, D., "Suspected Pulmonary Carcinogens in Environmental Tobacco Smoke," Environ Tech Letters 9: 539-544, 1988.

6. Aviado, D., "Health Effects of 50 Selected Constituents of Environmental Tobacco Smoke." In: Indoor Air Quality. H. Kasuga (ed.). Berlin, Heidelberg, Springer-Verlag, 383-389, 1990.

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PHILIP MORRIS RESPONSE TO OSHA RFI

Question 13(a): "Have these factors been considered in instances where IAQ investigations have failed to identify a specific contaminant source?

(b) If yes, was remedial action taken to improve these conditions? Please explain what that action was.

(c) Did health complaints decline?"

Summary:

Sick building investigation databases indicate the important role of so-called physical stressors such as temperature, lighting, noise, and ergonomics in perceived worker satisfaction with the working environment. Job satisfaction, security, and type of work also are important factors in perceived worker comfort. Tobacco smoke, because it is visible and easily identifiable, is often identified as a "stressor" in the work environment. However, investigations reveal that reported complaints about tobacco smoke may be misdirected and the result of less obvious conditions such as lack of ventilation (stuffy air), high temperatures, inadequate lighting, overcrowding and uncomfortable working conditions. Increased outdoor ventilation, as well as adequate temperature and humidity control, have resulted in a decrease in worker complaints about IAQ.

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PHILIP MORRIS RESPONSE TO OSHA RFI

Question 13(a): "Have these factors been considered in instances where IAQ investigations have failed to identify a specific contaminant source?

(b) If yes, was remedial action taken to improve these conditions? Please explain what that action was.

(c) Did health complaints decline?"

Response:

Sick building investigation databases indicate the important role of so-called physical stressors such as temperature, lighting, noise, and ergonomics in perceived worker satisfaction with the working environment.[1-8] Job satisfaction, security, and type of work also are important factors in perceived worker comfort.[9-13] Tobacco smoke, because it is visible and easily identifiable, is often identified as a "stressor" in the work environment. However, investigations reveal that reported adverse response to tobacco smoke may be misdirected and a result of less obvious conditions such as lack of ventilation (stuffy air), high temperatures, inadequate lighting, overcrowding and uncomfortable working conditions.[1-13] Increased outdoor ventilation, as well as adequate temperature and humidity control, have resulted in a decrease in worker complaints about IAQ.

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REFERENCES*

1. Melius, J., et al., "Indoor Air Quality -- the NIOSH Experience," Ann Am Conf Gov Ind Hyg 10: 3-7, 1984.

2. Robertson, G., "Source, Nature and Symptomology on Indoor Air Pollutants." In: Indoor and Ambient Air Quality. R. Perry and P. Kirk (eds.). London, Selper Ltd., 311-319, 1988.

3. Kirkbride, J., Sick Building Syndrome: Causes and Effects, Health and Welfare Canada, Ottawa, Canada, October 24, 1985.

4. Collett, C., et al., "A Database of Problem Buildings: Learning by Past Mistakes." In: Present and Future of Indoor Air Quality. C. Bieva, et al. (eds.). Amsterdam, Elsevier Science Publishers, 413-419, 1989.

5. Sterling, T. and Sterling, E., "Investigations on the Effect of Regulating Smoking on Levels on Indoor Pollution and on the Perception of Health and Comfort of Office Workers." In: ETS - Environmental Tobacco Smoke: Report from a Workshop on Effects and Exposure Levels. R. Rylander, Y. Peterson and M.C. Snella (eds.). Published simultaneously in European Journal of Respiratory Diseases, Supplement No. 133, Vol. 65, 17-31, 1984.

6. Sterling, T., et al., "Environmental Tobacco Smoke and Indoor Air Quality in Modern Office Work Environments," Journal of Occupational Medicine 29(1): 57-62, 1987.

7. Kirkbride, J., et al., "Health and Welfare Canada's Experience in Indoor Air Quality Investigation." In: Indoor Air '90: Proceedings of the Fifth International Conference on Indoor Air Quality and Climate. Toronto, Canada, Volume 5, 99-106, July 29-August 3, 1990.

8. U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health, Division of Standards Development and Technology Transfer, "The NIOSH Approach to Conducting Indoor Air Quality Investigations in Office Buildings," Indoor Air Quality Selected References, September, 1989.

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* Copies of listed references are supplied in the Philip Morris Response to RFI Question No. 3.

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9. Pimm, P., et al., "Physiological Effects of Acute Passive Exposure to Cigarette Smoke," Arch Environ Health 33(4): 201-213, 1978.

10. Winneke, G., et al., "Psychophysiological Response to Environmental Tobacco Smoke in an Experimental Social Setting." In: Indoor Air Quality. H. Kasuga (ed.). Berlin, Heidelberg, Springer-Verlag, 173-183, 1990.

11. Sterling, T.D., et al., "Building Illness in the White-Collar Workplace," International Journal of Health Services 3: 277-287, 1983.

12. Skov, P., et al., "Influence of Personal Characteristics, Job-Related Factors and Psychosocial Factors on the Sick Building Syndrome," Scand J Environ Health 15: 286-295, 1989.

13. Colligan, M., "The Psychological Effects of Indoor Air Pollution," Bulletin of the New York Academy of Medicine 57: 1014-1026, 1981.

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PHILIP MORRIS RESPONSE TO OSHA RFI

Question 14: "If your company keeps records of employee IAQ complaints, can you summarize your experience, emphasizing your efforts to localize the problem, identify the contaminants, determine the adverse health effects, and action taken?"

Summary:

Philip Morris retains information on specific IAQ investigations that have been conducted, although few IAQ complaints have been recorded. To localize potential problems, an investigation usually begins in an area where employees have complained of symptoms (e.g., eye, nose or throat irritation, dizziness, headache or nausea). A preliminary walk-through is conducted, to determine if any ongoing processes could be contributing a contaminant to the work area. This is followed by a visual survey of the HVAC system in that area, to determine the supply and exhaust layout and the quantities of air supplied to the work area. The HVAC system is checked to ensure that it is operating properly and to determine the percentage of fresh make-up air. Air filters and condensate collection pans are also examined. When environmental measurements are conducted, substances measured may include oxygen, carbon dioxide, carbon monoxide, formaldehyde and ozone.

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PHILIP MORRIS RESPONSE TO OSHA RFI

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Response:

Philip Morris retains information on specific IAQ investigations that have been conducted, although few IAQ complaints have been recorded. To localize potential problems, an investigation usually begins in an area where employees have complained of symptoms (e.g., eye, nose or throat irritation, dizziness, headache or nausea). A preliminary walk-through is conducted, to determine if any ongoing processes could be contributing a contaminant to the work area. This is followed by a visual survey of the HVAC system in that area, to determine the supply and exhaust layout and the quantities of air supplied to the work area. The HVAC system is checked to ensure that it is operating properly and to determine the percentage of fresh make-up air. Air filters and condensate collection pans are also examined. When environmental measurements are conducted, substances measured may include oxygen, carbon dioxide, carbon monoxide, formaldehyde and ozone.

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